เอกสารประกอบการสอน

วิชา 313 712 Endocrinology of Domestic Animals เรื่อง Gastrointestinal Hormones and Applications in Farm Animals



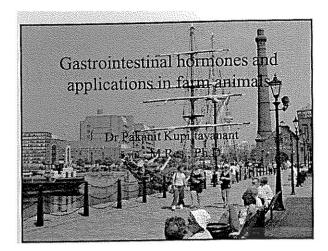
โดย

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คำนำ

เอกสารประกอบการสอนนี้จัดทำขึ้นเพื่อใช้ประกอบการเรียนการสอนในรายวิชา 313 712 Endocrinology of Domestic Animals เรื่อง Gastrointestinal Hormones and Applications in Farm Animals ให้กับนักศึกษาระดับบัณฑิตศึกษาของสาขาวิชา เทคโนโลยีการผลิตสัตว์ มหาวิทยาลัยเทคโนโลยีสุรนารี หวังว่าเอกสารนี้จะเป็นประโยชน์ต่อ การศึกษาในด้าน Endocrinology แก่นักศึกษาและผู้สนใจทั่วไป

ผศ.น.สพ.ดร. ภคนิจ คุปพิทยานันท์ เมษายน 2555



Contents

- · Actions of GI hormones
- Source and chemistry of the gastrointestinal hormones
- The gastrin family of hormones
- · The secretin family of hormones
- · Other candidate hormones

Actions of gastrointestinal hormones

- The action of gastrointestinal hormones are primarily concerned with
 - the digestion
 - and movement of food products along the GI tract
- They release the enzymes necessary to split specific food substrates, such as
 - proteins, carbohydrates, and fats, into their simpler components, amino acids, sugars, and fatty acids respectively.

- The GI hormones also enhance the activity of enzymes by stimulating the secretion of acid which provides the pH optimum for enzymatic action
- Hormonal stimulation of bile salt secretion provides the medium in which fat globulescan become emulsified, thus increasing the surface area for enzymatic activity
- · Thus, the major role of the GI hormones is
 - to facilitate the conversion of food substrates into molecular forms that then can gain access into the bloodstream

Source and chemistry of the gastrointestinal hormones

- The GI hormonrs are synthesized within system of clear cells (enterochromaffin, argyrophil, or argentaffin cells)
- These clear cells, scattered within the GI tract mucosa from the stomach through the colon, are often referred to as the diffuse or dispersed endocrine system, or along with the pancreatic hormones, as the gastroenteropancreatic hormones

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- The enterochromaffinlike (ECL) cells of the gut and pancreas have been classified as deriving from certain cell types, designed, for example as D(somatostatin), G(gastrin), or S(secretin)
- Based on their homology of structure, the gut hormones can be conveniently grouped into twos families. The gartrin family, and the secretin family

The gastrin family of hormones

- The gastrin family comprises the gastrins and the cholecystokinins (CCK)
- The C-terminal five amino-acid sequences of gastrin and CCK are identical

Structures of the gastrin family of hormone

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Observation by Ala-Pro-Sur-On-Ang-Val-Sur-Men-Men-Men-Up-LyA-Aco-Lou-Lin-Sur-Lu-Lu-Lu-Pro-Sur-Mis-Ang-No-Sur-Asp-Ang-Asp-Ang-Men-Our-Ing-Mast-Asp-Pro-Sur-

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18 19 50 21 22 23 24 25 26 27 28 59 50 31 32 34

Figure 10.1 Amino acid sequences of human G-17 graten and chologystokinin (CCK), identical Control participation sequences are indicated.

The secretin family of hormones

- The secretin family consists of secretin, glucagon, vasoactive intestinal polypeptide (VIP), and gastric inhibitory peptide (GIP)
- Secretin is semilar to glucagon in structure:
 14 of the 27 amino acids of secretin are semilar to those found in glucagon, which is 29 amino acids long

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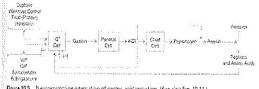
The structure of GIP and VIP possess many amino acids in common with those found in glucagon and secretin	
Structures of the secretin family of hormone 1 2 4 5 6 7 8 9 30 10 13 13 14 This behavior of the secretin family of hormone 1 3 6 6 7 8 9 30 10 10 20 14 14 This behavior of the secretin family of hormone 1 3 6 6 7 18 12 20 21 21 22 24 25 25 25 25 25 25 25 25 25 25 25 25 25	
Other candidate hormones • They bear no structural similarity to each other or to the other GI hormones • Include - Motilin - Somatostatin - Substance P - Neurotensin - Gastric-releasing peptide	

Physiological roles of the gastrointestinal hormone	
Gastrin	*** **********************************
Castini	
Gastrin	
- Was isolated in 1964	, · · · · · · · · · · · · · · · · · · ·
An antral hormone controlling gastric acid (HCl) secretion	
- The antral mucosa of the stomach is the richest source	7-07-04-04-04-1
of gastrin in all investigated species	
Gastrin is present in the gastric juice, which has aroused speculation that gastrin might be release from	
the ruminal surface, as well as from the basal surface into the blood	
into the blood	
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(4)	
Food is the primary physiological stimulus	
of gastrin secretion	
- Peptide fragments, amino acids, and to a lesser	
extent FFAs are stimulatory to gastrin secretion	
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Gastrin secretion is under ANS control	
- For example, in some species, the vagus nerve	
stimulates gastrin secretion in anticipation of the ingestion of food or through activation of	
local neural reflexes following distention of the	
stomach after food intake	
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- · One physiological function of gastrin is to stimulate hydrochloric acid (HCl) and pepsinogen secretion within the fundus of stomach
- · Gastrin does not stimulate pepsinogen secretion directly, but rather indirectly, through release of
- · In other words, hydrogen ions from the acid are stimulatory to pepsinogen secretion from the chief

Stimulus and endocrine cell

Neuroendocrine integration of gastric acid secretion



Secretin

- Secretin is one of peptide hormone of the small intestine
- The tissues concentration of secretin diminishes from duodenum to ileum
- Secretinlike immunoreactivity is localized to the granular S cells, which are present between the crypts and villi of the mucosa of the small intestine

- Acidification of the duodenal mucosa, resulting from HCl arriving in the duodenum from the stomach, is the normal stimulus for secretion
- At a pH above 4.5, secretin is not released in sufficient amounts to stimulate pancreatic bicarbonate(NaHCO₃) secretion.

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- Secretin stimulates pancreatic secretion of HCO₃ into the duodenum; the HCO₃ neutralizes the H+ from the stomach, which raises the pH, hence decreasing the release of secretin, which removes any further stimulus to bicarbonate secretion
- The clearly defined roles of secretin are to stimulate pancreatic bicarbonate secretion and to potentiate CCK-stimulated pancreatic enzyme secretion

Homeostatic closed-loop endocrine mechanism of small intestine pH control Secreta Parices Musicos 14,503 (Recensidation: Parices (Recensidation: Parices pH control.

Cholecystokinin (CCK)

- Is liberated by food (particularly lipids) and caused contraction and emptying of the gallbladder
- CCK = pancreozymin (PZ)

· Structure:

- Is a polypeptide hormone of 33-amino-acid residues
- The carboxyterminal five amino acid from the carboxyterminus is sulphated, which is necessary for the normal physiological activity of the molecule
- All terminal forms off CCK are important in stimulating pancreatic enzyme secretion and gallbladder contraction

· CCK:

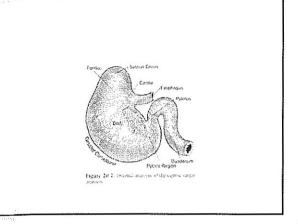
- Is immunocytochemically localized to the I cells of the duodenal, jejunal, and ileal mucosa
- Is released by L-isomers of amino acids, hydrochloric acid, and certain fatty acids
- Entry of high levels of hydrogen ion into duodenum results in gall bladder contraction, specific biological response attributed to circulating CCK

· Physiological roles:

- Contraction of the gallbladder mediated by CCKinduced release of acetylcholine
- Relaxation of sphincter of Oddi mediated by CCKinduced release of VIP
- Inhibition of gastric emptying mediated by CCK-induced activation of an inhibitory vago-vagal reflex involving vasoactive intestinal peptide-induced relaxation of gastric fundus
- Other recognized physiological role of CCK are stimulation of pancreatic enzyme secretion

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Liver: Associated Structures Galbhadder Right and her bepate ducts of liver With folds Cystic duct Discolenum Associated Structures Bio duct and applicate Cystic duct Major discolence Major discolence



Gastric inhibitory peptide (GIP)

- · Is a 43 amino acid peptide hormone
- Is localized to certain K cells of duodenum & iejunum
- Is stimulated by fat ingestion, glucose, HCl, amino acid in the lumen
- · Has an inhibitory effect on gastric secretion
- Is insulinotrophic potentiating insulin release in response to an intravenous infusion of glucose

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· Action:

- Has an inhibitory effect on gastric secretion
- Is insulinotrophic potentiating insulin release in response to an intravenous infusion of glucose
- Is a potent stimulator of pancreatic water and electrolyte secretion from the duodenal gland
- Has direct metabolic effects on other tissues and organs (adipose tissue, liver, muscle, GI tract, and brain)
 - · Adipose tissue: inhibit lipolysis
 - · GI tract: increase electrolyte secretion

Vasoactive intestinal peptide (VIP)

- · Contains 28 amino acid residues
- · Relaxes a variety of smooth muscles
- Antagonises the effects of smooth muscle constrictor agents
- Inhibits histamine and pentagastrinstimulates gastric acid secretion
- Increases electrolyte and water secretion from pancreas and bile flow

Somatostatin

- Is localized to specialized D cells of the GI mucosa
- · Is also found in peripheral and CNS nerves
- Inhibits gastric secretion of acid and pepsinogen, pancreatic secretion of enzyme
- Blocks the secretion and stimulates the absorption of electrolytes in the small intestine

Motilin

- Is found in the intestinal mucosa of mammals
- · Contains 22 amino acid residues
- Present in highest concentration in the duodenum
- · Stimulates gastric motor activity
- Stimulate GI motility and emptying of chyme into the small intestine

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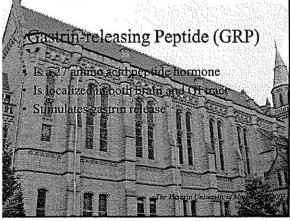
Neurotensin

- Produced by gut endocrine cells and neurons in the brain
- · Considered as a hormone mediator for:
 - Inhibition of gastric secretion
 - Stimulation of pancreatic and intestinal fluid secretion
 - Changes in intestinal motility from fasting to fed pattern

Substance P

- · Consists of 11 amino acid residues
- Is found in nerve fibers in all areas of the GI wall
- · Is also found in the brain
- Acts as smooth muscle modulation of smooth muscle activity in gut tissue (peristalsis)





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GIP .	 gastric acid secretion; ? glucose mediated in take selvens.
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Applications

- · Cholecystokinin (CCK) and appetite
- Mechanism of action → CCK inhibits food intake (appetite) of domestic animals
- The capacity of pigs for growth is limited to some extent by the amount of feed they consume, so methods for increasing appetite should increase weight gain and shorten the time take to reach slaughter weight

 Feed intake is increased by stimulation of the lateral hypothalamic nuclei, while stimulation of the ventral medial hypothalamus decreases feed intake

 Cells within these regions have glucoreceptors that monitor blood glucose levels to control feed intake

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• Other hormones or metabolites may also affect the feeding and satiety centers in the hypothalamus • One such hormone is cholecystokinin (CCK) · CCK or related peptide also acts as an important satiety signal to reduce food intake So interfering with CCK function can be used to increase food intake · Differences in plasma levels of CCK have been found in pigs with different genetic potential for feed intake · This suggests that satiety effects of CCK are involved in the genetic differences between lines of pigs for feed intake • In human, increased levels of CCK, or sensitive to CCK, have been implicated in age-related anorexia [/]วั_{กยาลัยเทคโนโล} · CCK may also prove useful in the control of obesity in humans • Immunizing pigs, but not sheep against CCK-8 increased growth rate by about 10% and feed intake by 8%, with no change in carcass composition. Antibody titres were highly variable and were correlated with weight gain (McCauley et al., 1995)

 Treatment of pigs and immature rainbow trout with a CCK(A) receptor antagonist (MK-329) increased feeding behaviour, feed intake and weight gain (Bernad et al., 2000)

