

เอกสารประกอบการสอน

วิชา 313 712 Endocrinology of Domestic Animals

เรื่อง Gastrointestinal Hormones and Applications in Farm Animals



โดย

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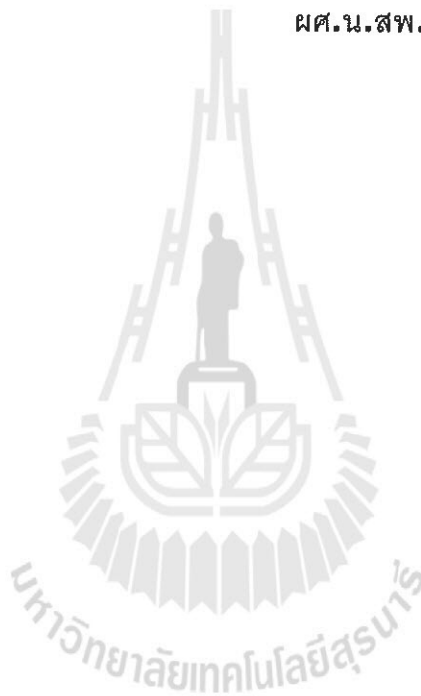
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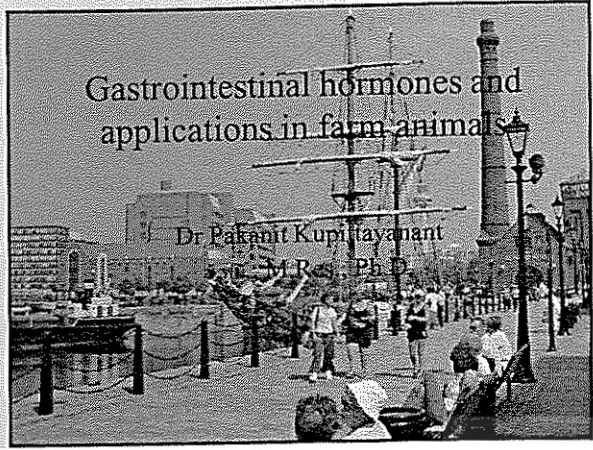
คำนำ

เอกสารประกอบการสอนนี้จัดทำขึ้นเพื่อใช้ประกอบการเรียนการสอนในรายวิชา 313 712 Endocrinology of Domestic Animals เรื่อง Gastrointestinal Hormones and Applications in Farm Animals ให้กับนักศึกษาระดับบัณฑิตศึกษาของสาขาวิชาเทคโนโลยีการผลิตสัตว์ มหาวิทยาลัยเทคโนโลยีสุรนารี หวังว่าเอกสารนี้จะเป็นประโยชน์ต่อการศึกษาด้าน Endocrinology แก่นักศึกษาและผู้สนใจทั่วไป

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Gastrointestinal hormones and applications in farm animals

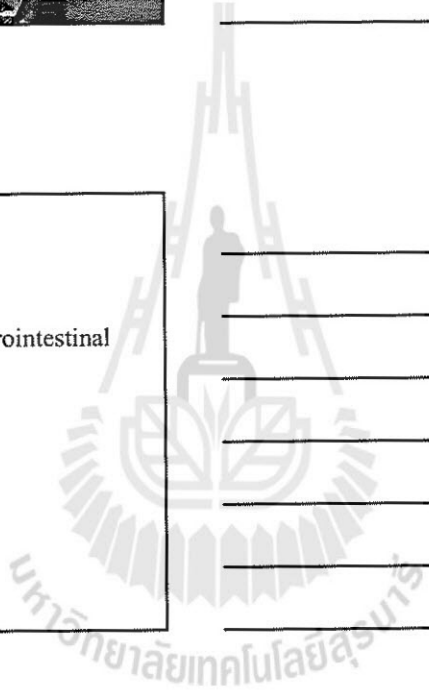
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Contents

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

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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.

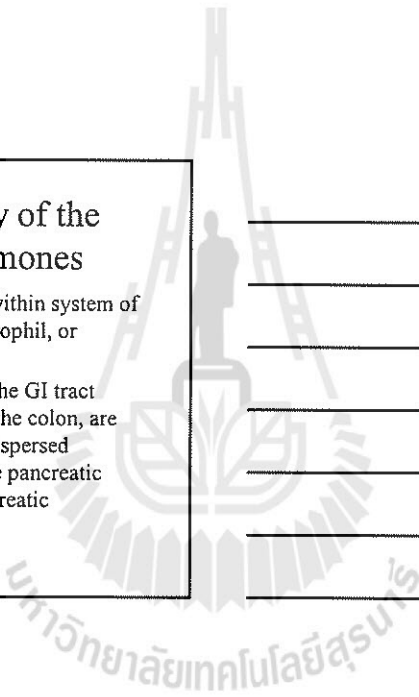
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- The GI hormones also enhance the activity of enzymes by stimulating the secretion of acid which provides the pH optimum for enzymatic action
- Hormonal stimulation of bile salt secretion provides the medium in which fat globules can become emulsified, 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 hormones 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



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

- 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	3	4	5	6	7	8	9	10	11	12	13	14
GIP	His	Ser	Arg	Asp	Val	Thr	Met	Thr	Leu	Asn	Pro	Leu	Leu	Arg
Secretin	His	Ser	Arg	Gly	Thr	Pro	Thr	Thr	Ser	Asp	Leu	Leu	Leu	Arg
Glucagon	His	Ser	Gly	Gly	Thr	Pro	Thr	Thr	Ser	Asp	Leu	Leu	Leu	Arg
VIP	Trp	Asp	Arg	Gly	Thr	Pro	Thr	Thr	Ser	Asp	Leu	Leu	Leu	Arg

	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
GIP	Arg	Pro	His	Met	Asp	Val	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu
Secretin	Arg	Pro	His	Met	Asp	Val	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu
Glucagon	Arg	Pro	His	Met	Asp	Val	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu
VIP	Arg	Pro	His	Met	Asp	Val	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu

Figure 10.2 Amino acid sequences of peptide hormones of the secretin family. Black-filled areas indicate identical amino acid residues between peptides.

Other candidate hormones

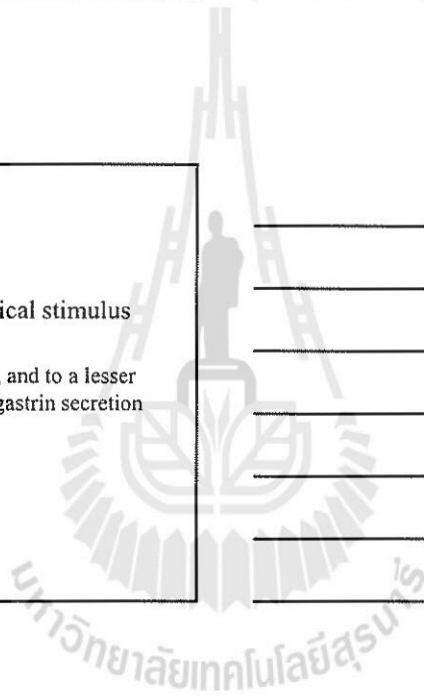
- They bear no structural similarity to each other or to the other GI hormones
- Include
 - Motilin
 - Somatostatin
 - Substance P
 - Neurotensin
 - Gastric-releasing peptide

Physiological roles of the gastrointestinal hormone
Gastrin

- Gastrin
 - Was isolated in 1964
 - An antral hormone controlling gastric acid (HCl) secretion
 - The antral mucosa of the stomach is the richest source of gastrin in all investigated species
 - Gastrin is present in the gastric juice, which has aroused speculation that gastrin might be released from the ruminal surface, as well as from the basal surface into the blood

- Food is the primary physiological stimulus of gastrin secretion
 - Peptide fragments, amino acids, and to a lesser extent FFAs are stimulatory to gastrin secretion

- 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

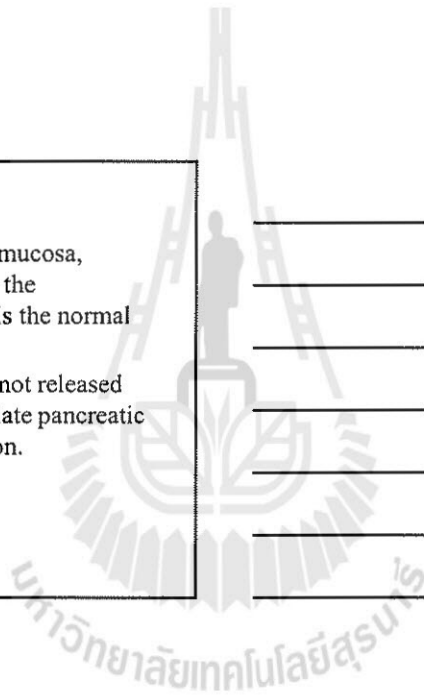


Secretin

- 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 secretin secretion
- At a pH above 4.5, secretin is not released in sufficient amounts to stimulate pancreatic bicarbonate(NaHCO_3) secretion.

- Secretin stimulates pancreatic secretion of HCO_3 into the duodenum; the HCO_3 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



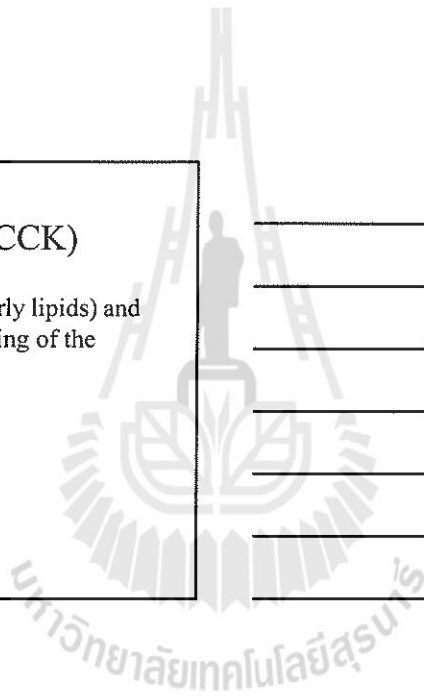
Homeostatic closed-loop endocrine mechanism of small intestine pH control



Figure 10.6 Homeostatic closed-loop endocrine mechanism of small intestine pH control.

Cholecystokinin (CCK)

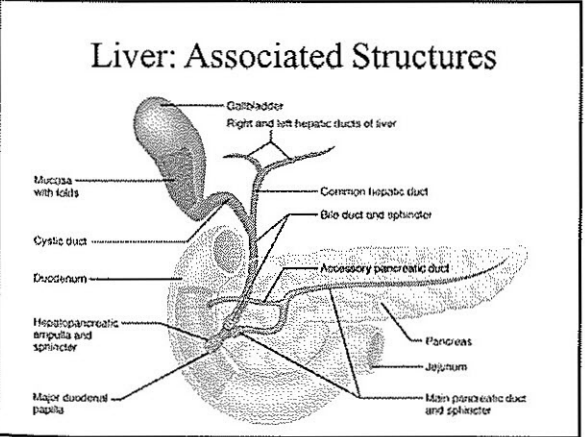
- Is liberated by food (particularly lipids) and caused contraction and emptying of the gallbladder
- CCK = pancreozymin (PZ)

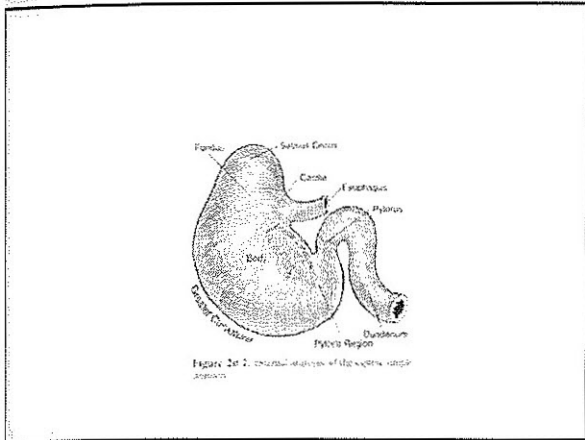


- Structure:
 - Is a polypeptide hormone of 33-amino-acid residues
 - The carboxyterminal five amino acid from the carboxyterminus is sulphated, which is necessary for the normal physiological activity of the molecule
 - All terminal forms off CCK are important in stimulating pancreatic enzyme secretion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

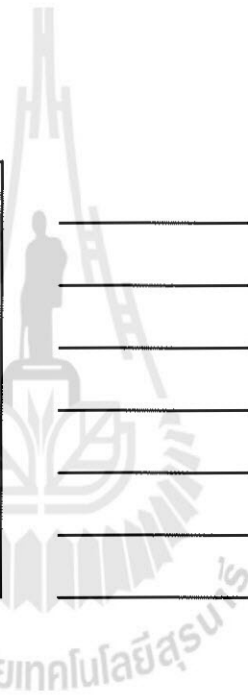
- Physiological roles:
 - Contraction of the gallbladder mediated by CCK-induced release of acetylcholine
 - Relaxation of sphincter of Oddi mediated by CCK-induced release of VIP
 - Inhibition of gastric emptying mediated by CCK-induced activation of an inhibitory vago-vagal reflex involving vasoactive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





Gastric inhibitory peptide (GIP)

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



- Action:
 - Has an inhibitory effect on gastric secretion
 - Is insulinotropic - 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)

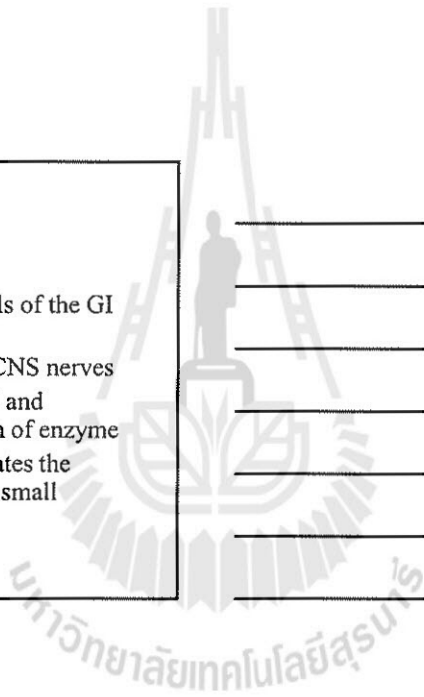
- Contains 28 amino acid residues
- Relaxes a variety of smooth muscles
- Antagonises the effects of smooth muscle constrictor agents
- Inhibits histamine and pentagastrin-stimulates gastric acid secretion
- Increases electrolyte and water secretion from pancreas and bile flow

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



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

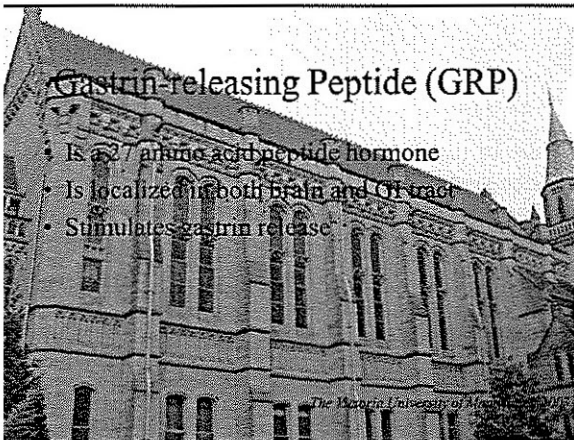
Substance P

- 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)



Gastrin-releasing Peptide (GRP)

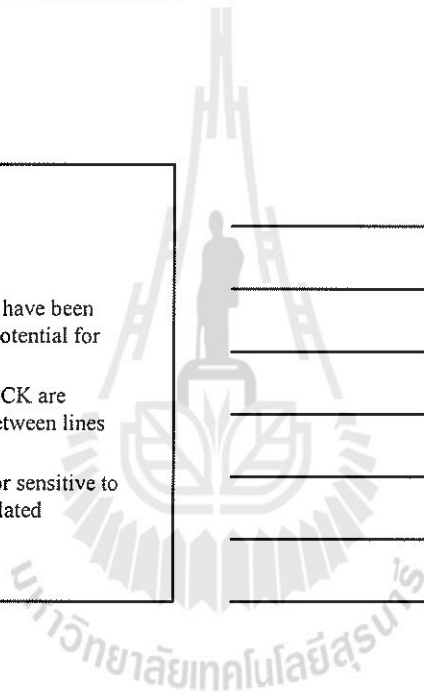
- Is 27 amino acid peptide hormone
- Is localized in both brain and GI tract
- Stimulates gastrin release



- 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

- 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*)

