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Pancreas

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Pancreas: Pancreas act as dual organ performing two functions such as endocrine and exocrine. Endocrine function is related to the production of hormones, whereas the exocrine function is related to the secretion of digestive juice termed as 'pancreatic juice'.

Functional Anatomy of exocrine part of pancreas: Exocrine part of pancreas is similar to salivary gland regarding structure. It consists of acini or alveoli. Each acinus consists of a simple layer or acinar cells with a lumen in the center. Acinar cells consist of zymogen granules, which exhibit digestive enzymes. A small duct is derived from the lumen of each alveolus. Some of these ducts particularly from neighbouring alveoli combine to form intralobular duct. All the intralobular ducts lead to the formation of main duct of pancreas termed as wirsung duct. Wirsung duct combines with common bile duct and results in the formation of ampulla of Vater, which gains an entry into duodenum. In a very few persons, an accessory duct known as Santorini duct is also seen. The duct of Santorini also opens into duodenum, proximal to the opening of ampulla of Vater.

Nerve supply to pancreas: Pancreas is supplied by both sympathetic as well as parasympathetic fibers. Sympathetic fibres are supplied through splanchnic nerve whereas parasympathetic fibers are supplied through vagus nerve.

Properties and composition of pancreatic juice: Pancreatic juice has the following properties.

pH: More alkaline with a pH of 8.0 to 8.3.

Specific gravity: 1.010 to 1.018

Volume: 500 - 800ml/ day

Composition of pancreatic juice: Pancreatic juice consists of 99.5% of water and 0.5% of solids. The solids include both organic as well as inorganic compounds. Composition of pancreatic juice is given in Table 1.

Table 1. **Composition of pancreatic juice:**

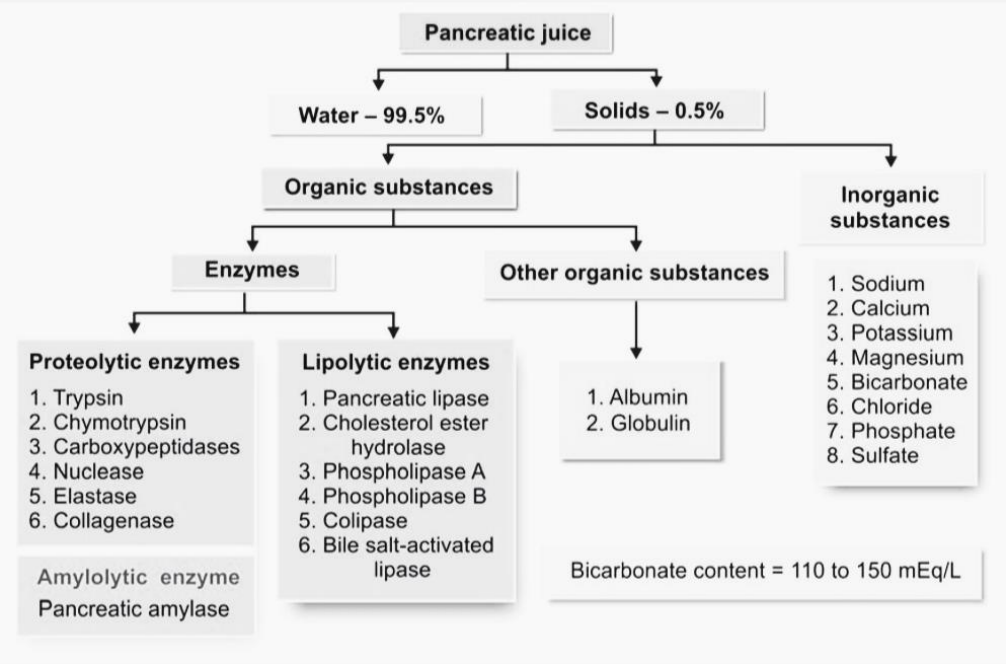
Pancreatic juice consists of more bicarbonate content, which is approximately 110 to 150mEQ/L. against the plasma level bicarbonate of 24mEQ/L. Bicarbonates in pancreatic juice is essential for two major reasons:

- Pancreatic juice shows more alkalinity because of the presence of high bicarbonates, which protects intestinal mucosa by neutralising the acid chyme.
- Bicarbonate ions confer the required pH of 7 to 9, which is optimal for the activation of pancreatic enzymes.

Functions of pancreatic juice: Pancreatic juice exhibits digestive functions as well as acid neutralising action.

Digestive functions of pancreatic juice: Pancreatic juice plays an essential role in the digestion of proteins and lipids. However, pancreatic juice has only mild digestive action on carbohydrates.

Digestion of proteins: Trypsin and chymotrypsin are treated as major proteolytic enzymes of pancreatic juice. Other proteolytic enzymes include carboxypeptidase, collagenase, lactase and nuclease.



Trypsin: Trypsin is a single polypeptide with a molecular weight of 25,000 Da, and consists of 229 amino acids. The secretion of trypsin occurs as inactive trypsinogen, which is changed into active trypsin with the help of enterokinase. Enterokinase is also known as enteropeptidase, and is secreted by the brush border cells of duodenal mucus membrane. Immediately after secretion, trypsin stimulates trypsinogen due to an autocatalytic action.

Trypsin inhibitor: Activation of trypsinogen occurs only in the small intestine. If activation of trypsin occurs in pancreas, trypsin hydrolyse pancreatic tissue proteins and leads to pancreatic damage. Trypsin inhibitor, also known as inhibitor protein, obstructs the activation of trypsin particularly in the acini, ducts of pancreas and secretory cells. Any abnormality of the trypsin inhibitor leads to an unopposed trypsin activity, which destroys the pancreas.

Physiological actions of trypsin:

1. **Auto catalytic action:** After formation, trypsin converts trypsinogen to trypsin.
2. **Blood clotting:** Trypsin enhances blood clotting.
3. **Curdling of milk:** Trypsin changes caseinogen in the milk to casein.

4. **Digestion of proteins:** Trypsin is a strong proteolytic enzyme. Trypsin is an endopeptidase and cleaves the interior bonds of the protein molecules and converts them into peptides and polypeptides.
5. Trypsin also stimulates collagenase, phospholipase A and phospholipase B.
6. Trypsin stimulates other enzymes of pancreatic juice namely, Chymotrypsinogen into chymotrypsin; Procarboxypeptidases into carboxypeptidases; Proelastase into elastase and Prolipase into lipase.

2. Chymotrypsin: Chymotrypsin is a polypeptide with a molecular weight of 25,700 Da. and consists of 240 amino acids. The secretion of chymotrypsin occurs as inactive Chymotrypsinogen, which is activated into chymotrypsin with the help of trypsin (Table 4).

Physiological actions of chymotrypsin:

- **Digestion of milk:** Chymotrypsinogen is capable of digesting caseinogen at a rapid rate when compared to trypsin. Combination of both enzymes are responsible for rapid digestion of milk
- **Digestion of proteins:** Chymotrypsin is also an endopeptidase and it changes proteins to polypeptides.

3. Carboxypeptidases: Carboxypeptidases include both carboxypeptidase A and carboxypeptidase B. Procarboxypeptidase A gives rise to carboxypeptidase A, and Procarboxypeptidase B gives rise to carboxypeptidase B. Procarboxypeptidases are activated into Carboxypeptidases with the help of trypsin (Table 4).

Physiological actions of Carboxypeptidases:

- Carboxypeptidases are exopeptidases and catalyse the terminal bond of protein molecules. Exopeptidases convert the polypeptides and other proteins into amino acids.
- Carboxypeptidase A breaks the proteins into amino acids that have aromatic or aliphatic side chains.
- Carboxypeptidase B changes the proteins into amino acids that have basic side chains.

4. Collagenase: Collagenase is secreted as an inactive procollagenase, which is then changed into collagenase.

5. Elastase: Elastase is sereted as an inactive proelastase which is then changed into elastase by trypsin. Elastase is able to digest the elastic fibres.

6. Nucleases: Nucleases of pancreatic juice are ribonuclease and deoxyribonuclease, which digests nucleic acids. These enzymes change ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) into component nucleotides (Table 4).

Digestion of lipids: Pancreatic juice consists of lipolytic enzymes such as pancreatic lipase, cholesterol ester hydrolase (CEH), phospholipase A, phospholipase B, bile salt activated lipase and colipase.

- **Bile salt activated lipase:** Bile salt activated lipase is the lipolytic enzyme stimulated with the help of bile salt. It is otherwise known as carboxy ester lipase or cholesterol esterase. This enzyme shows a weak lipolytic action when compared to pancreatic lipase. But it breaks down a number of lipids including cholesterol esters, phospholipids and triglycerides. Human milk consists of an enzyme similar to bile salt activated lipase.
- **Colipase:** Colipase is a small coenzyme. The secretion of Colipase occurs as inactive procolipase. Procolipase yields Colipase with the help of trypsin. Colipase enhances digestive action of pancreatic lipase on fats.
- **Cholesterol ester hydrolase:** Cholesterol ester hydrolase or cholesterol esterase changes cholesterol ester into free cholesterol as well as fatty acid via. hydrolysis.
- **Pancreatic lipase:** pancreatic lipase is a powerful lipolytic enzyme. It catalyses triglycerides into monoglycerides and fatty acids. Activity of pancreatic lipase is enhanced with the help of bile. Optimum pH needed for the activity of this enzyme is 7 to 9. Digestion of fat by pancreatic lipase needs two additional factors.
    1. Bile salts are essential for the emulsification of fat.
    2. Colipase, which is a coenzyme required for the pancreatic lipase to digest the dietary lipids is also needed. Pancreatic lipase is capable of digesting 80% of the fat, and absence or deficiency of this enzyme results in the elimination of undigested fat in the feces (steatorrhea).
- **Phospholipase A:** phospholipase A is stimulated by trypsin. Phospholipase A digests phospholipids such as cephalin and lecithin and changes them into lysophospholipids. It changes lecithin into lysolecithin as well as cephalin into lysocephalin.
- **Phospholipase B:** phospholipase B is also stimulated by Trypsin. It changes lysophospholipids, lysolecithin and lysocephalin, to phosphoryl choline as well as free fatty acids (FAA) (Table 2, 4).

Digestion of carbohydrates:

Pancreatic amylase is the amylolytic enzyme present in pancreatic juice. Similar to salivary amylase, the pancreatic amylase also changes starch into dextrin and maltose (table 2)

Neutralizing action of pancreatic juice: The pancreatic juice with high bicarbonate concentration is released into the intestine at the same time when acid chyme reaches intestine. Pancreatic juice is highly alkaline because of the presence of more quantity of bicarbonate ions. Hence, pancreatic juice is capable of neutralizing destructive action of acid in the chyme.

Mechanism of pancreatic secretion:

Secretion of pancreatic enzymes: The synthesis of pancreatic enzymes occurs in rough endoplasmic reticulum of acinar cells in the pancreas. The raw materials for the synthesis are the amino acids, which are derived from the blood. After synthesis, the enzymes are packed into zymogen granules with the help of Golgi apparatus and stored in the cytoplasm. When activated, the zymogen granules are released by the acinar cells into the pancreatic duct. From these granules, emerges the enzymes needed for digestion of food ingredients in the intestine.

Secretion of bicarbonate ions: The secretion of bicarbonate ions into pancreatic juice occurs from the cells of pancreatic ductules and pancreatic duct.

Mechanism of bicarbonate secretion:

- Carbondioxide derived from blood or metabolic process reacts with water inside the cell forms carbonic acid with the help of carbonic anhydrase.
- Carbonic acid dissociates into hydrogen as well as bicarbonate ions.
- Bicarbonate ions are transported actively out of the cells into the lumen.
- Hydrogen ions in blood are transported into the cell in exchange for sodium ion.
- Sodium ions then reacts with bicarbonate to form sodium bicarbonate.
- Due to the loss of sodium and bicarbonate ions from the blood, osmotic equilibrium of blood changes. To correct osmotic equilibrium, water then leaves the blood and enters into the lumen of pancreatic duct by simple osmosis.
- In the lumen, bicarbonate reacts with water.

Regulation of pancreatic secretion: Secretion of pancreatic juice is controlled by both neural and hormonal factors.

Stages of pancreatic secretion: Pancreatic juice is secreted in 3 stages such as cephalic phase, gastric phase and intestinal phase (Table 3). These 3 phases of pancreatic secretion are similar to the 3 phases of gastric secretion.

1. **Cephalic phase**: Similar to gastric secretion, cephalic phase is also controlled by neural reflex actions.

Two types of reflex actions are observed.

- Unconditioned reflex
- Conditioned reflex.

A. Unconditioned reflex: Unconditioned reflex is the inborn reflex. When food is kept in the mouth, salivary and gastric secretions will be initiated. Simultaneously, pancreatic secretion also starts.

Stages of reflex action:

- Presence of food in the mouth activates the taste buds and other receptors in the mouth.
- Afferent (sensory) impulses from mouth arrive at the dorsal nucleus of Vagas and efferent (motor) impulses reach pancreatic acini via. vagal efferent nerve fibres.
- Vagal efferent nerve endings produce acetylcholine, which activates pancreatic secretion.

B. Conditioned reflex: Conditioned reflex is a result of previous experience. Presence of food in the mouth is not essential to elicit this reflex. The sight, smell, word or thought of a food causes salivary, gastric and pancreatic secretions.

Stages of reflex action:

- Impulses from the special sensory organs such as eye, ear and nose pass through afferent (sensory) fibres of neural circuits to cerebral cortex directly. Thinking of food activates the cerebral cortex directly.
- From cerebral cortex, the impulses pass through Dorsal nucleus of vagus, vagal efferent fibers and reach pancreatic acini.
- Vagal nerve endings produce acetylcholine, which enhances pancreatic secretion.

2. **Gastric phase:** Secretion of pancreatic juice is observed when food enters the stomach. This is termed as gastric phase, which is under the control of gastrin hormone. If food enters stomach, the secretion of gastrin occurs from stomach. If gastrin is transported to pancreas through blood, it activates the pancreatic secretion, which contains more enzymes.

3. Intestinal phase: Intestinal phase is the secretion of pancreatic juice when the chyme enters the intestine. This phase is also under hormonal regulation. When chyme enters the intestine, a group hormones are released. A few of these activates the pancreatic secretion, while few others inhibit the pancreatic secretion.

Hormones activating pancreatic secretion: Cholecystokinin is a key hormone in this process.
Cholecystokinin: Cholecystokinin is also known as cholecystokinin- pancreozymin. Cholecystokinin is secreted by I cells present in duodenal as well as jejunal Mucosa. The stimulant for release of this hormone is the chyme containing peptides, amino acids and fatty acids. Cholecystokinin activates the secretion of pancreatic juice, which contains more enzymes and less volume, by acting on the pancreatic acinar cells with the help of inositol triphosphate (IP3, second messenger).

Hormones inhibiting pancreatic secretion:

- Pancreatic polypeptide produced by PP cells in islets of Langerhans of pancreas.
- Peptide like Ghrelin and Leptin.
- Peptide secreted by intestinal mucosa.
- Somatostatin secreted by D cells in the islets of Langerhans of pancreas.

Table 3: **Regulation of pancreatic secretion**

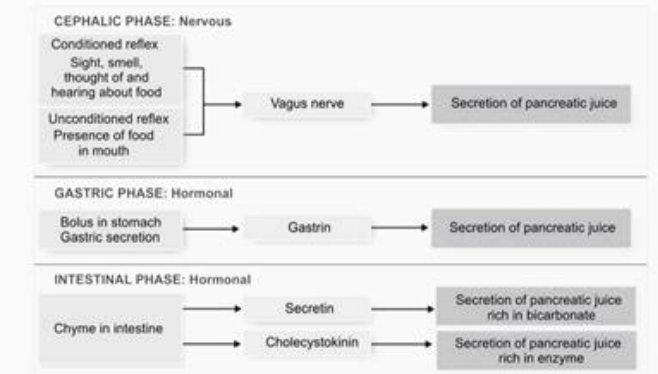


Table 4: Digestive enzymes of pancreatic juice:

Enzyme	**Activator**	**Acts on Substrate**	**End products**
Carboxypeptidases	Trypsin	Polypeptides	Amino acids
Cholesterol ester hydrolase (CEH)	Alkaline medium	Cholesterol ester	Cholesterol and fatty acids
Collagenase	Trypsin	Collagen	Amino acids
Colipase	Trypsin	Facilitates action of pancreatic lipase	
Bile-salt-activated lipase	Trypsin	Phospholipids Cholesterol esters Triglycerides	Lysophospholipids Cholesterol and fatty acids Monoglycerides and fatty acids
Chymotrypsin	Trypsin	Protein	Polypeptides
Elastase	Trypsin	Elastin	Aminoacids
Nuclease	Trypsin	DNA and RNA	Mononucleotides
Pancreatic lipase	Alkaline medium	Triglycerides	Monoglycerides and fatty acids
Phospholipase A	Trypsin	Phospholipids	Lysophospholipids
Phospholipase B	Trypsin	Lysophospholipids	Phosphoryl choline and free fatty acids

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