Revised & Approved

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BIOCHEMISTRY TEAM
439

MED439
KING SAUD UNIVERSITY

Biochemical aspects of digestion of proteins and carbohydrates

Editing File

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Objectives

- Understand the overall process of dietary proteins' and carbohydrates' digestion, the organs involved, the enzymes required, and the end products

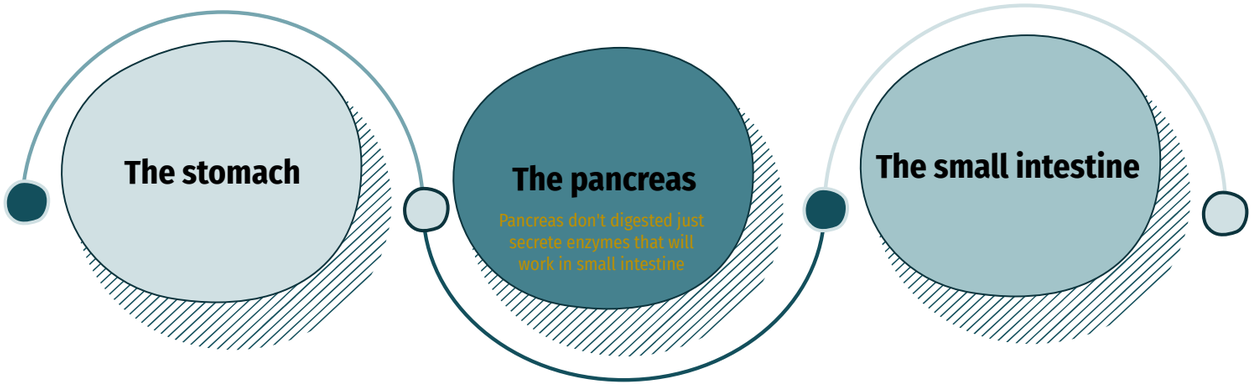
- Implement the basic science knowledge of the process of proteins & carbohydrates digestion to understand the clinical manifestations of diseases that involve defective proteins' or carbohydrates' digestion &/or absorption.

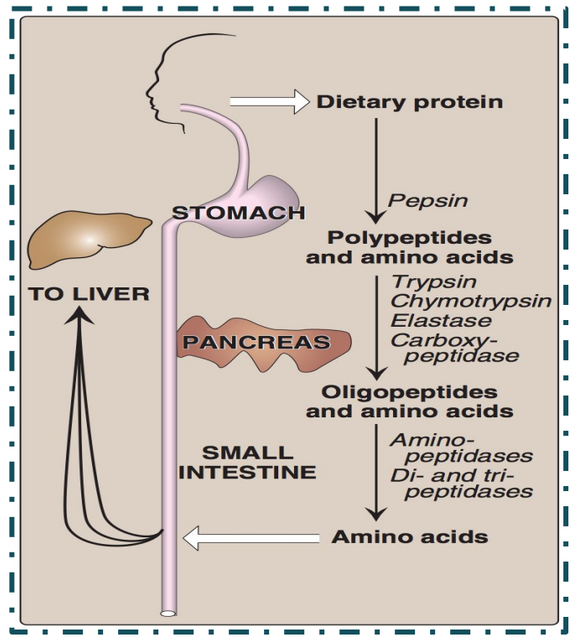
Protein Digestion

- Dietary proteins constitute 70-100 g/ day.
- Proteins are generally too large to be absorbed by the intestine
  - The only protein that can be absorbed by the intestine is the maternal antibodies
- They must, therefore, be hydrolyzed to their constituent amino acids, which can be absorbed

The Source of Proteolytic Enzymes Responsible for Degrading Dietary Proteins

Digestion of protein not starts in the mouth





Digestion of proteins by gastric secretion

The gastric juice contains 2 components important for protein digestion:

- Hydrochloric acid
- Pepsin In the stomach HCL activates pepsinogen to pepsin, pepsin in turn will activate more and more pepsin, a process called autocatalysis

Digesting agent	Description
Hydrochloric acid	1. kills some bacteria 2.Denatures proteins→denatured proteins are more susceptible to hydrolysis by proteases. Doesn't break bonds, only denature proteins, Return to primary structure
Pepsin	•Acid stable •Endopeptidase Endopeptidase is removing amino acid from the middle, and Exopeptidase is removing amino acid from N terminal or C terminal. •Secreted as inactive zymogen (pepsinogen) Zymogen: inactive substance which is converted into an enzyme when activated by another enzyme •Pepsinogen is activated by: 1. hydrochloric acid 2. pepsin, i.e. autocatalysis •Protein digestion by stomach→Polypeptides + few free amino acids

Digestion of proteins in small intestine

Digestion by pancreatic enzymes

Digestion by intestinal aminopeptidase

The digestion in small intestine is hormonally controlled

Two small peptide hormones are released from cells of the upper part of small intestine:
1-Cholecystokinin (CKK)
2- Secretin

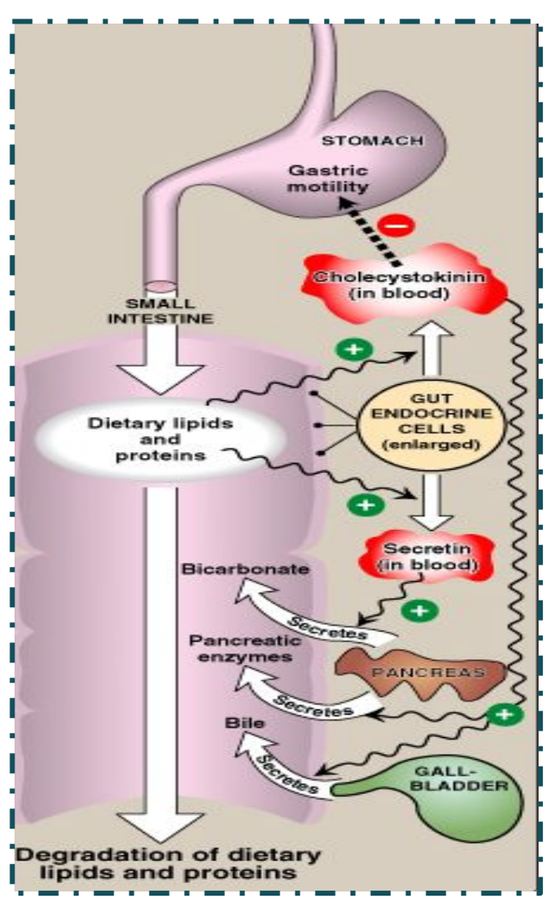
Hormonal control of digestion in small intestine:

Cholecystokinin (CKK)

- Secretion of pancreatic enzymes.
- Bile secretion.
- Slow release of gastric contents

Secretin

- Release of watery solution rich in bicarbonate by pancreas



The gut hormones

Gut hormone	Stimulus for secretion	Effects
Cholecystokinin (CCK)	The presence of partially digested proteins (& lipids) in the upper small intestine. Once the food move as chyme from the stomach to the small intestine it will activate CCK	1. Stimulates the release of pancreatic digestive enzymes 2. Stimulates the contraction of the gallbladder & release of bile (bile is used for lipids) 3. Decreases gastric motility → slower release of gastric contents into the small intestine (to give more time for the digestion)
Secretin	Low pH of the chyme entering the intestine 1- The presence of chyme in low pH in the small intestine will stimulate Secretin. 2- After that the Secretin will give an order to the Pancreas to secrete substances that rich in Bicarbonate, why? because enzymes **not** work in acidity.	Stimulates the pancreas to release a watery solution rich in bicarbonate to neutralize the pH of the intestinal contents (to reach the optimum pH for digestive activity by pancreatic enzymes)

Pancreatic enzymes for digestion of proteins

- The pancreatic secretion contains a group of pancreatic proteases
- Each of these enzymes has different specificity for the cleavage sites
  They have certain specificity so they recognize certain amino acid, and don't break the peptide bonds randomly
  For example: Between arginine and lysine there's a peptide bond, this peptide bond is specific for them not others.
- These proteases are synthesized and secreted as inactive zymogens
  Just like Pepsinogen it was inactive then it will be converted into the active form.

Activation of pancreatic enzymes

Enteropeptidase Converts trypsinogen to trypsin.

Trypsin then activates all the other pancreatic zymogens (including itself)

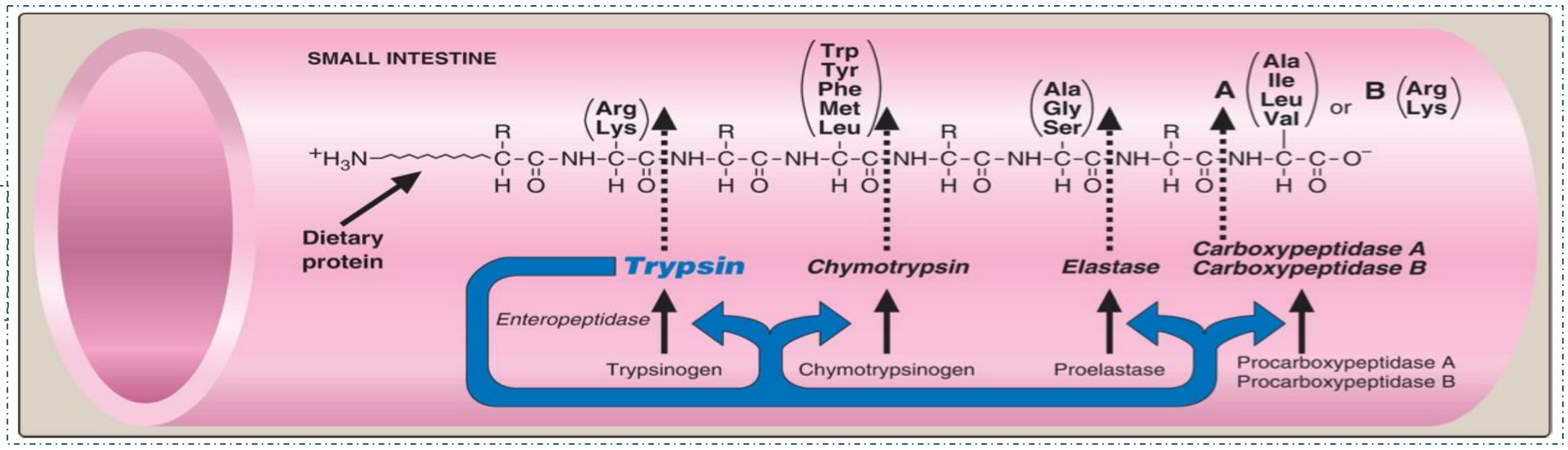
Enteropeptidase is an enzyme synthesized by, and present on the luminal surface of intestinal mucosal cells of the brush border membrane

Pancreatic proteases

Break polypeptides into oligopeptides

Zymogen	Active enzyme		Activating enzyme
Trypsinogen	Trypsin	Endopeptidase Break peptide bonds within the molecule	1- Enteropeptidase 2- Trypsin (autocatalysis)
Chymotrypsinogen	Chymotrypsin		Trypsin
Proelastase	Elastase		Trypsin
Procarboxypeptidases	Carboxypeptidases	Exopeptidases Break peptide bonds from end-pieces of terminal amino acids	Trypsin

Enteropeptidase activates trypsinogen into trypsin, trypsin then can activate pancreatic enzymes including trypsin itself -autocatalysis



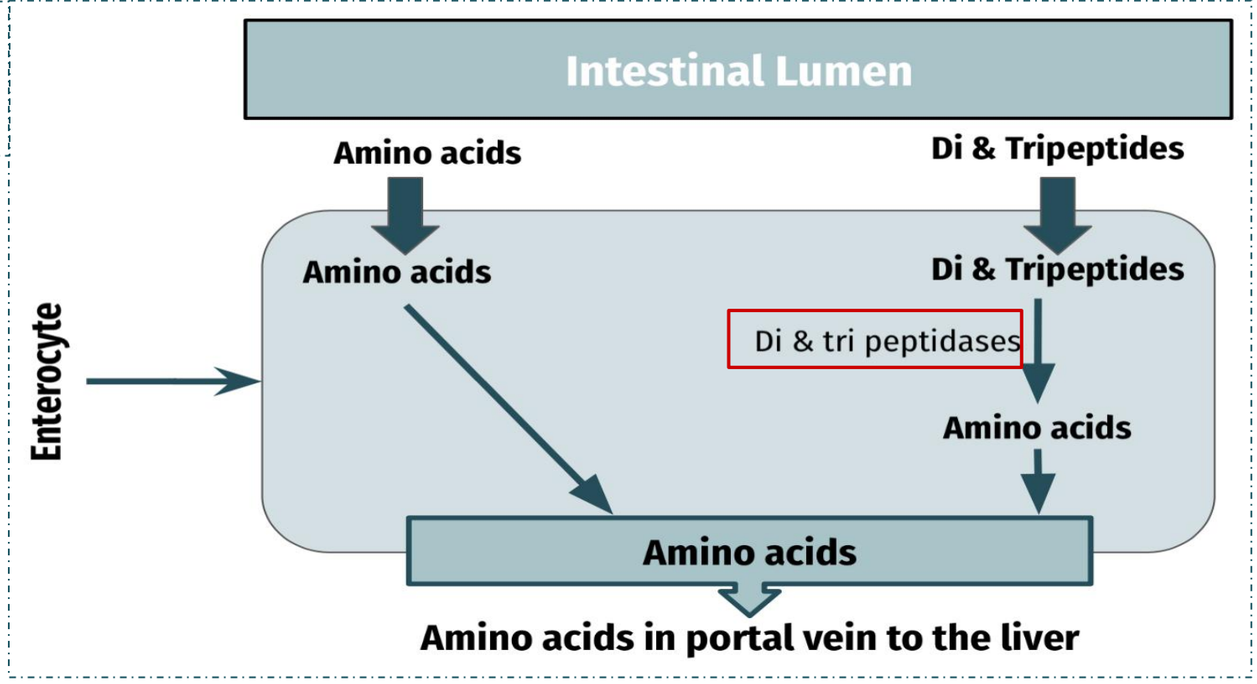
Digestion of proteins in small intestine: continued ...

Digestion by intestinal aminopeptidase

Oligopeptides that result from the action of pancreatic proteases are cleaved into free amino acids and smaller peptides (di- & tri- peptides) by **intestinal aminopeptidase** (an exopeptidase on the luminal surface of the intestine)

Absorption of digested proteins

In the intestinal lumen, absorption of dipeptides and tripeptides require enzymes (di and tri peptidase)



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Genetic Errors in Amino Acids Transport

if there is a mutation in the transporter of amino acid, it may lead to a disease.

Cystinuria is an inherited disease causes loss of amino acids and are identified in urine, the amino acid are Cystine, Ornithine, Lysine and arginine

Cystinuria

Cys**teine**: is a sulfur-containing amino acid.
Cys**tine**: is formed from two cysteine molecules joined together

explanation from Team 435:
Because the small intestine and the proximal tubule of the kidney have common transport systems, a defect in any one of these systems results in an inability to absorb particular amino acids into the gut and into the kidney tubules.
For example, one system is responsible for the uptake of **cystine** and the dibasic amino acids (which are amino acids that have another amino group in their side chains, so the have 2 bases – 2 amino groups - : **ornithine**, **lysine**, **arginine** (represented as "**COLA** ").
In the inherited disorder **cystinuria**, this carrier system is defective, and all four amino acids appear in the urine. The disease expresses itself clinically by the precipitation of cystine to form kidney stones (calculi), which can block the urinary tract

About the disease — **Cystinuria** is one of the most common genetic error of amino acid transport.

Example of — Inherited disorder in the **transport** of certain amino acids.

Affects — transport of **Cystine and dibasic** amino acids.

Organs affected — the **small intestine** **Absorption** will be affected in the intestine so it will be excreted out of the body **and the kidney** Kidney will reduce absorption of **(cystine,ornithine,lysine,arginine)**. That's why it called cystin**uria**

Clinically — Cystine and dibasic amino acids appear in the urine and there is kidney **stones formation**.

Management Not imp. — Oral **hydration** (drinking lots of water) is an important part of treatment (to prevent kidney stones formation).

Abnormalities of protein digestion

Pancreatic insufficiency, e.g., chronic pancreatitis, cystic fibrosis, surgical removal of the pancreas

↓

Incomplete digestion & absorption of lipids & proteins

↓

Abnormal appearance of lipids (steatorrhea) & undigested proteins in the feces

Definition:
It is a disease of malabsorption resulting from immune mediated damage to the villi of the small intestine in response to ingestion of gluten.
The antibodies are against gliadin, a protein made of metabolism of gluten

Celiac Disease (Celiac sprue)

Celiac disease is a hereditary disorder caused by sensitivity to the gliadin fraction of gluten, a protein found in wheat; similar proteins are present in rye and barley. In a genetically susceptible person, gluten-sensitive T cells are activated when gluten-derived peptide epitopes are presented. The inflammatory response causes characteristic mucosal villous atrophy in the small bowel.

Gluten is a protein found in wheat, rye, and barley.

Biochemical aspects of digestion of dietary carbohydrate

Carbohydrates Digestion:

Rapid digestion because it starts in the mouth
(physical chewing and alpha amylase enzyme) No carbs digestion in the stomach (due to high acidity)

Carbohydrates digestion is rapid: Generally completed by the time the gastric contents reach the junction of the duodenum & jejunum.
After neutralization of pH by secretin, the chyme now is in the intestines with more neutral pH and more enzymes are ready to start to work, this happens in the duodenum and upper jejunum

Sites for digestion of dietary carbohydrates:

- The mouth
- The intestinal lumen

Dietary Carbohydrates Mainly:

Monosaccharides

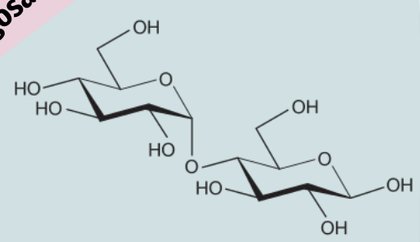
Little amounts

Dietary food contains little amounts of monosaccharides because it's expensive in the food industry

Disaccharides

- **Sucrose**
- **Lactose**
- **Maltose**

Oligosaccharides



The structure is Extra

Polysaccharides

Contain alpha(1-4) & alpha (1-6) bonds :

- Starch from plant origin
- Glycogen from animal origin

Contain beta(1-4) bonds:

- Cellulose from plant origin

Cellulose is not absorbed by the body because there is no enzyme that cleaves its bond -beta 1,4

Enzymes for Digestion of Dietary Carbohydrates

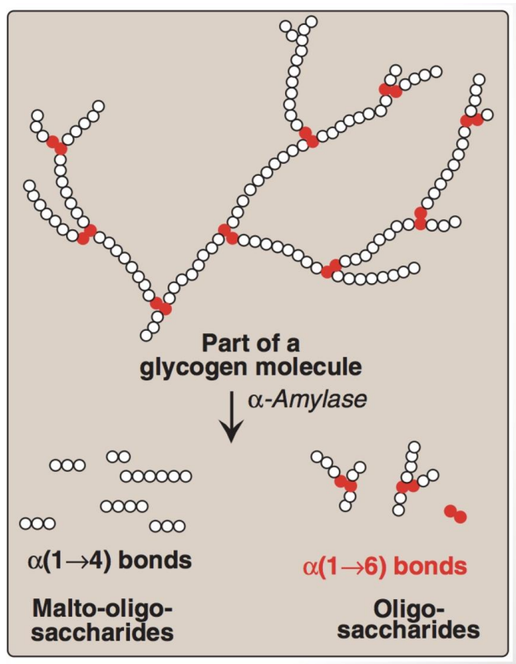
Enzymes

- **α-amylase**
  - -location:Both salivary &pancreatic.
  - -Substrate: Polysaccharides
- **Disaccharidases**
  - -location :Intestinal
  - -Substrate: Disaccharides
- **Isomaltase & α(1,6) glucosidase**
  - -location:Intestinal
  - -Substrate: Branch points of oligo- and di-saccharides

Effects of α-amylase on Glycogen

Hydrolysis of:
α(1,4) glycosidic bonds

Productes:
-Mixture of **short oligosaccharides** (both branched & unbranched)
-Disaccharides: **Maltose and isomaltose**



After every 8 to 10 amino acids we have a branch point

- **No dietary carbohydrate digestion occurs in the stomach**
  (the high acidity of the stomach inactivates the salivary α–amylase)
- **Pancreatic α–amylase continues the process of starch & glycogen digestion in the small intestine.**
  (Secreted by pancreas and works in small intestine)

Serum level of α-amylases

very important for OSPE

Normal level in serum: 25 -125 U/L

The clinical significance of **rising** circulating levels of **α-amylase activity:**

Diagnosis of acute pancreatitis:

(damage of pancreatic cells —> release & activation of the intracellular enzymes into the blood)

- Its level starts to rise within few hours
- Reaches a peak within 12- 72 hours.
- Then returns to normal within few days.

Final digestion of carbohydrates by intestinal enzymes in the small intestine

The mucosal lining of the **jejunum**

Location of their action:

Enzymes:

1- Disaccharidases

2- α(1,6) Glucosidase (for branched oligosaccharides)

Source:

Secreted by & remain associated with the luminal side of the brush border membranes of the intestinal mucosal cells

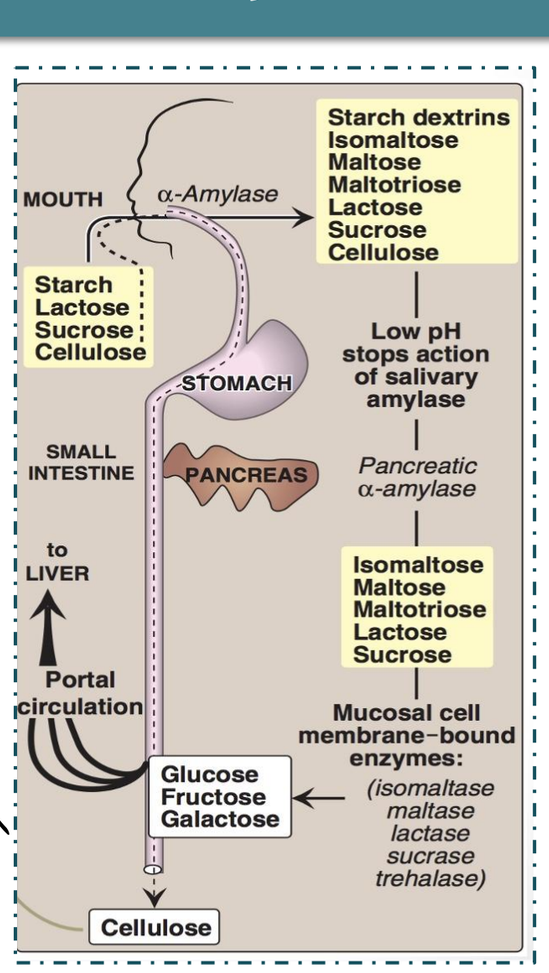
Intestinal disaccharidases

Table is important

Enzyme	Substrate	Product
Isomaltase	isomaltose	2 Glucose
Maltase	maltose	2 Glucose
Sucrase	sucrose	Glucose & fructose
Lactase (β-galactosidase)	lactose	Glucose & galactose

Digestion of Carbohydrates

Dietary cellulose cannot be digested due to the absence of enzyme that can cleave β (1-4)bonds. It passes through the GIT largely intact. despite that, it has several beneficial effects



Absorption of Monosaccharides by Intestinal Mucosal Cells

Location: Duodenum & upper jejunum.

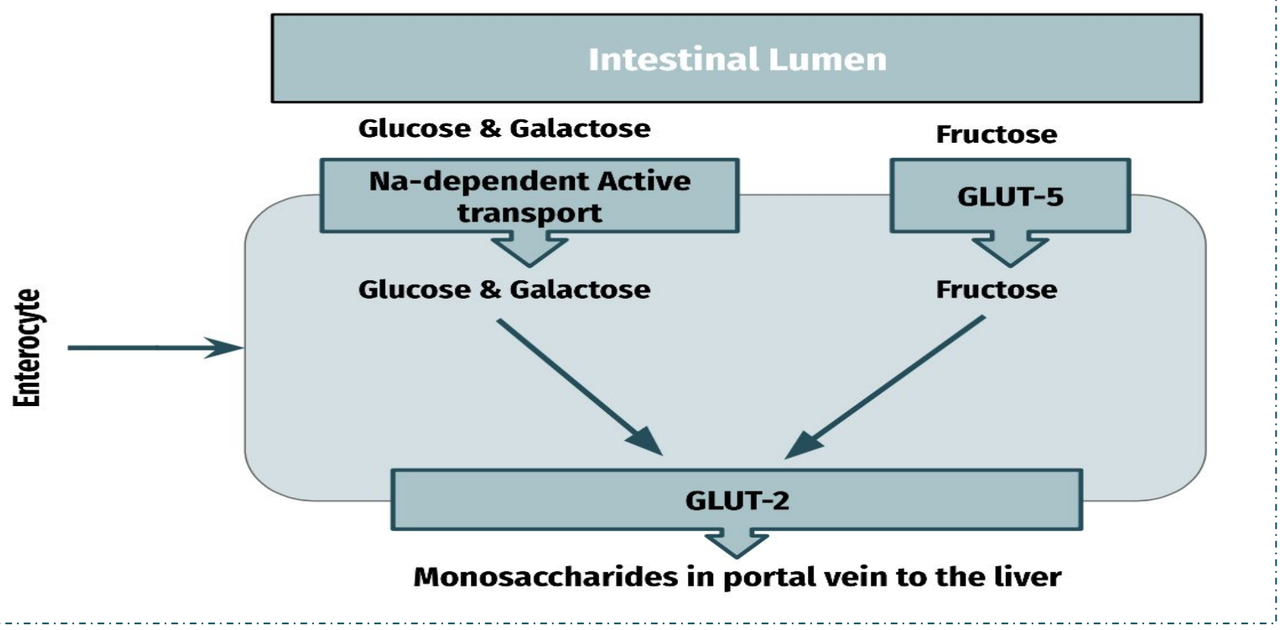
Insulin: is **NOT** required for the uptake of glucose by intestinal cells.

Different monosaccharides have different mechanisms of absorption:

- **Facilitated** diffusion (**GLUT**-mediated)
- **Active** transport (Energy-dependent): **Co-transport with Na^+**

Absorption of digested carbohydrates

-Fructose is carried to enterocytes by GLUT5
-Glucose and Galactose are carried by SGLT1 and SGLT2
They are carried from enterocytes to live by GLUT2



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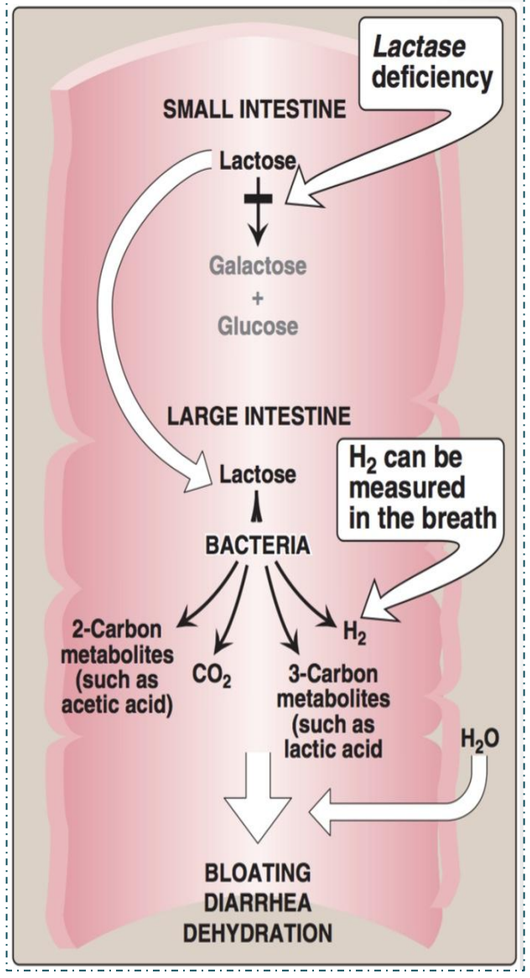
Abnormal digestion of disaccharides (e.g. of lactose)

In people who have lactose intolerance due to deficiency of Lactase, the GIT Normal flora utilizes lactose and causes the symptoms of intolerance like increase co2, diarrhea, distention, etc,

Lactose intolerance (Lactase deficiency)

Lactase (β-galactosidase) deficiency → Undigested carbohydrate in large intestine → osmotic diarrhea

Bacterial fermentation of the undigested compounds in the large intestine → CO_2 , H_2 gas → abdominal cramps, diarrhea & distension (flatulence)



Take Home Messages

- Proteolytic enzymes responsible for digestion of dietary proteins are produced by the stomach, the pancreas & the small intestine.
- The digestion of proteins in the stomach is the result of the action of HCl and pepsin.
- Pancreatic proteases are, like pepsin, synthesized and secreted as inactive zymogens.
- The intestinal digestion of proteins occurs in the small intestine's lumen, on the luminal surface of the small intestine, and is completed intracellularly to produce free amino acids.
- In pancreatic insufficiency, the digestion and absorption of fat & protein is incomplete → steatorrhea & appearance of undigested proteins in the feces.
- Salivary -amylase acts on dietary glycogen & starch in the mouth.
- Pancreatic -amylase continues the process of polysaccharide digestion in small intestine.
- The final digestive processes of carbohydrates into monosaccharides occur at the mucosal of lining of the small intestine by disaccharidases & (1,6) glucosidase.
- Dietary cellulose cannot be digested due to the absence of enzyme that can cleave β (1-4) bonds, so it passes through the GIT largely intact. Despite that, it has several beneficial effects.
- Absorption of the monosaccharides requires specific transporters (GLUTs).
- Lactose intolerance is due to deficiency of lactase enzyme and causes abdominal cramps, diarrhea & flatulence

Summary

	Protein Digestion	Carbohydrates Digestion	
Site	• The stomach • The pancreas • The small intestine	• The mouth • The intestinal lumen	

secretions	Gastric secretions:
	• HCL
	• Pepsin. Pepsinogen is activated by:
	  ○ hydrochloric acid
	  ○ pepsin, i.e. autocatalysis
	Intestinal digestion:
	• pancreatic enzymes (inactive zymogens)
	• Intestinal aminopeptidase
		• α-amylase
		• Disaccharidases
		• Isomaltase & a(1,6) glucosidase	

Activation of pancreatic enzymes	1. Enteropeptidase Converts trypsinogen to trypsin.
	2. Trypsin then activates all the other pancreatic zymogens (including itself):
	  a. Chymotrypsin (endopeptidase)
	  b. Elastase (endopeptidase)
	  c. Carboxypeptidases (exopeptidases)
		α-amylase	Normal level in serum: 25 -125 U/L
			significance**: Diagnosis of acute pancreatitis**

Hormonal control of digestion in small intestine	• **Cholecystokinin (CCK)** • **Secretin**	**Absorption of monosaccharides**	1. Facilitated diffusion (GLUT-mediated) 2. Active transport (Energy-dependent): Co-transport with Na^+
Abnormallties	1. **Cystinuria :** Genetic errors in Cystine and dibasic amino acids transport. 2. **celiac disease :** immune mediated damage to the villi of the small intestine in response to ingestion of gluten.	**Lactose intolerance**	

MCQs

1- Which of the following is not a source of Proteolytic Enzymes Responsible for Degrading Dietary Proteins?			
A- Kidney	B- Stomach	C- Pancreas	D- Small intestine
2- Which of the following is an active enzyme for Proelastase?			
A-Trypsin	B- Exopeptidase	C- Elastase	D- Endopeptidase
3- Which organ is affected by Cystinuria?			
A-Urethra	B- Colon	C-Small intestine	D- Stomach
4-which of the following is true about cellulose?			
A-contains α(1-6) bonds	B- It has an animal origin	C-It's an oligosaccharide	D-It contains β(1-4)bonds
5- where can α-amylase enzyme be found?			
A- salivary	B-Intestinal	C-pancreatic	D-both A and C
6-what is a product of the breakdown of lactose ?			
A- 2 glucose	B- glucose and galactose	C- glucose and fructose	D- fructose and galactose

Answers key

1- A 2- C 3- C 4- D 5- D 6- B

SAQs

1- What are some of the effects of Cholecystokinin (CCK)?

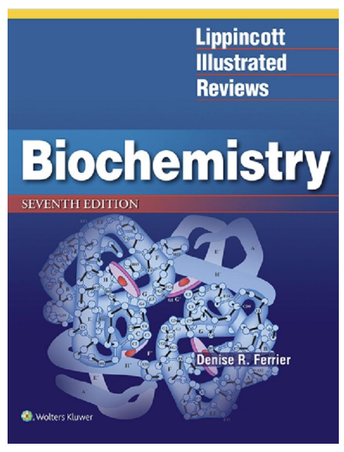
Answer
1. Stimulates the release of pancreatic digestive enzymes
2. Stimulates the contraction of the gallbladder & release of bile (bile is used for lipids)
3. Decreases gastric motility → slower release of gastric contents into the small intestine (to give more time for the digestion)

2- What is celiac disease (celiac sprue)?

It is a disease of malabsorption resulting from immune mediated damage to the villi of the small intestine in response to ingestion of gluten

Resources

Click on the book to download the resource



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