Biochemistry Team 435

جامعة الملك سعود
King Saud University 1957

DIGESTION OF PROTEINS AND CARBOHYDRATES.

* Please check out this link to know if there are any changes or additions.

Revised by
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Color index: Important | Doctors notes | Further explanation.

OBJECTIVES:

By the end of this lecture, the student should be able to:

- 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 and carbohydrates digestion to understand the clinical manifestations of diseases that involve defective proteins' or carbohydrates' digestion and/or absorption.

Part I: Biochemical Aspects of Digestion of Dietary proteins:

- Dietary proteins constitute :**70-100** g/day.
- Proteins are generally too large to be absorbed by the intestine. They must therefore be hydrolyzed to their constituent amino acids which can be absorbed.

The source of proteolytic enzymes responsible for degrading dietary proteins:

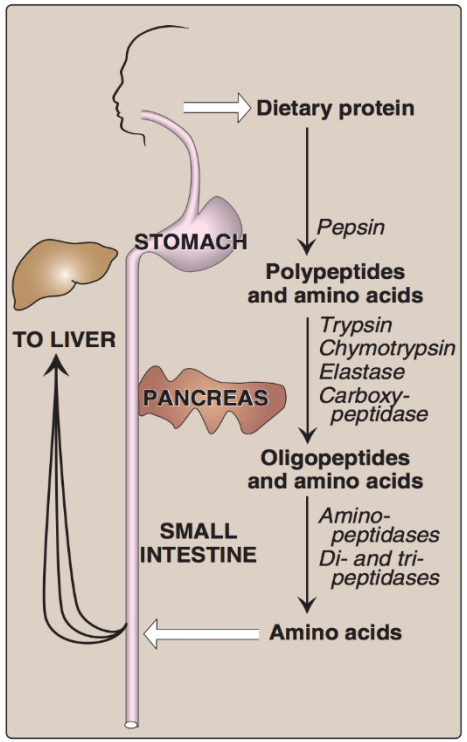
- The stomach
- The small intestine
- The pancreas

Digestion of proteins in Stomach:

- The digestion of proteins begins in the stomach which secrets **gastric juice**.
- A unique solution containing 2 components important for protein digestion:
  - **Hydrochloric acid (HCl).**
  - **Pepsin.**

In stomach, proteins get converted into primary structures (denaturing)

Digesting agent	Description
Hydrochloric Acid (HCl)	▪ kills some bacteria ▪ **Denatures proteins** → denatured proteins are more susceptible to hydrolysis by proteases.
Pepsin	▪ Acid-stable. ▪ Endopeptidase. "meaning was explained in first lecture". ▪ Secreted as **inactive zymogen** (**pepsinogen**) ▪ Pepsinogen is then activated by: 1. **hydrochloric acid.** 2. **pepsin** that have already been formed (autocatalysis). ▪ Protein digestion by stomach → **Polypeptides** + **few free amino acids**.



The source of proteolytic enzymes responsible for degrading dietary proteins:

- The stomach
- The small intestine
- The pancreas

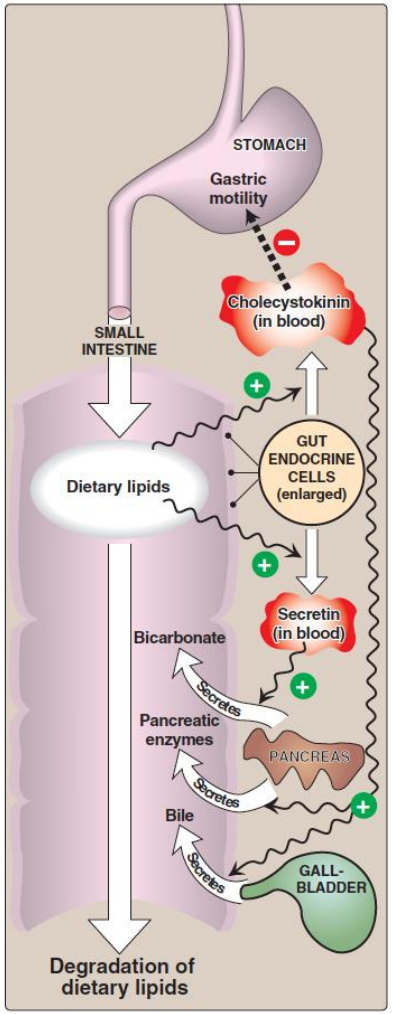
Digestion of proteins in Small intestine:

A. digestion by pancreatic enzymes.

B. 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**:

Hormone	Stimulus	Effects
1-Cholecystokinin (CCK)	The presence of **partially digested** proteins and lipids in the upper small intestine.	▪ Stimulates the **release of pancreatic digestive** enzymes ▪ Stimulates the contraction of the gall bladder and release of bile **"Bile secretion"**. ▪ Decreases gastric motility → **slower release of gastric** contents into the small intestine
2-Secretin	**Low pH** of the chyme entering the intestine	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).



The source of proteolytic enzymes responsible for degrading dietary proteins:

- The stomach
- The small intestine
- The pancreas

Digestion of proteins in Small intestine:

A. digestion by pancreatic enzymes.

- The pancreatic secretion contains a group of pancreatic proteases.
- Each of these enzymes has different **specificity** for the cleavage sites.

Pancreatic enzymes are very specific. For instance, trypsin will cut only if there is arginine or lysine.

- These proteases are synthesized and secreted as **inactive zymogens**.

In this step the polypeptide is broken into oligopeptides + amino acids by specific enzymes.

Zymogen	Active enzyme	Activating enzyme
Trypsinogen	Trypsin (endopeptidase)	1- Enteropeptidase 2- Trypsin (autocatalysis)
Chymotrypsinogen	Chymotrypsin (endopeptidase)	Trypsin
Proelastase	Elastase (endopeptidase)	Trypsin
Procarboxypeptidases **A & B**	Carboxypeptidases (**exopeptidases**)	Trypsin

الجدول مهم جدا!!!

Enteropeptidase:

An enzyme synthesized by and present on the luminal surface of intestinal mucosal cells of the brush border membrane

converts **trypsinogen** to **trypsin**

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

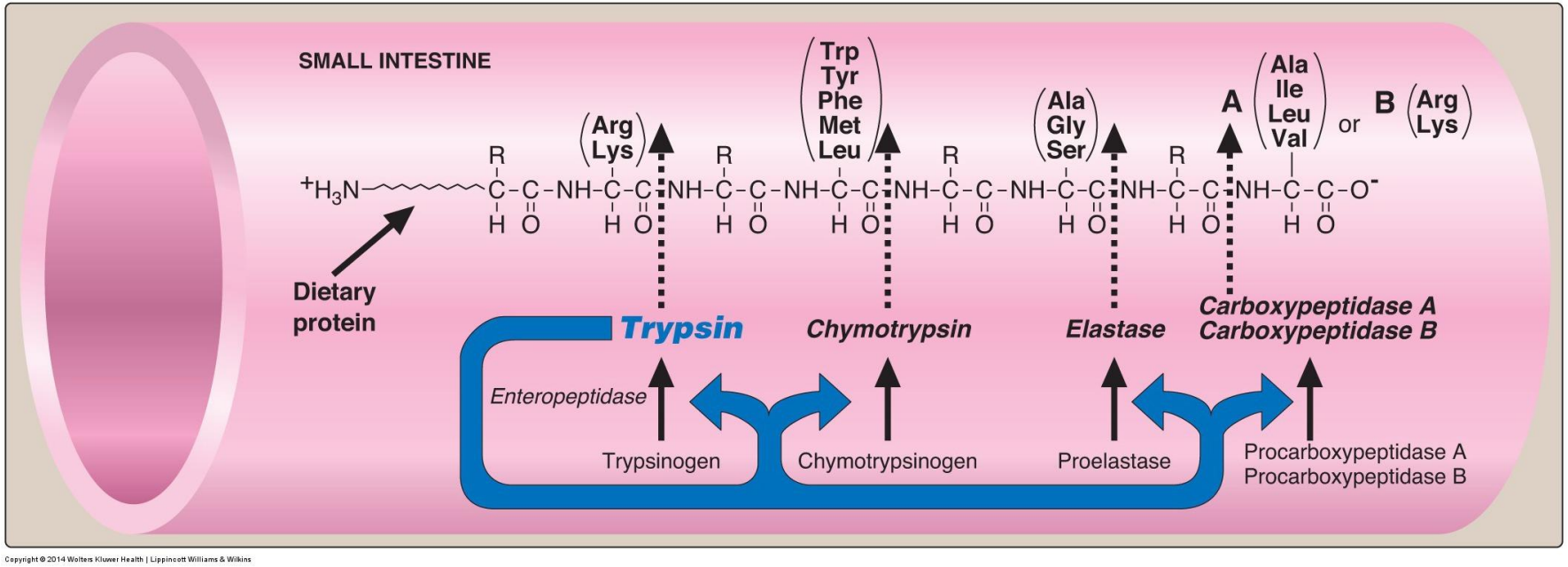
The source of proteolytic enzymes responsible for degrading dietary proteins:

- The stomach
- The small intestine
- The pancreas

Digestion of proteins in Small intestine:

A. digestion by pancreatic enzymes.

This picture summarizes all the information in the previous slide



cleavage of dietary protein in the small intestine by pancreatic proteases. The peptide bonds susceptible to hydrolysis are shown for each of the five major pancreatic proteases. [Note: The first three are serine endopeptidases, whereas the last two are exopeptidases. Each is produced from an inactive zymogen.]

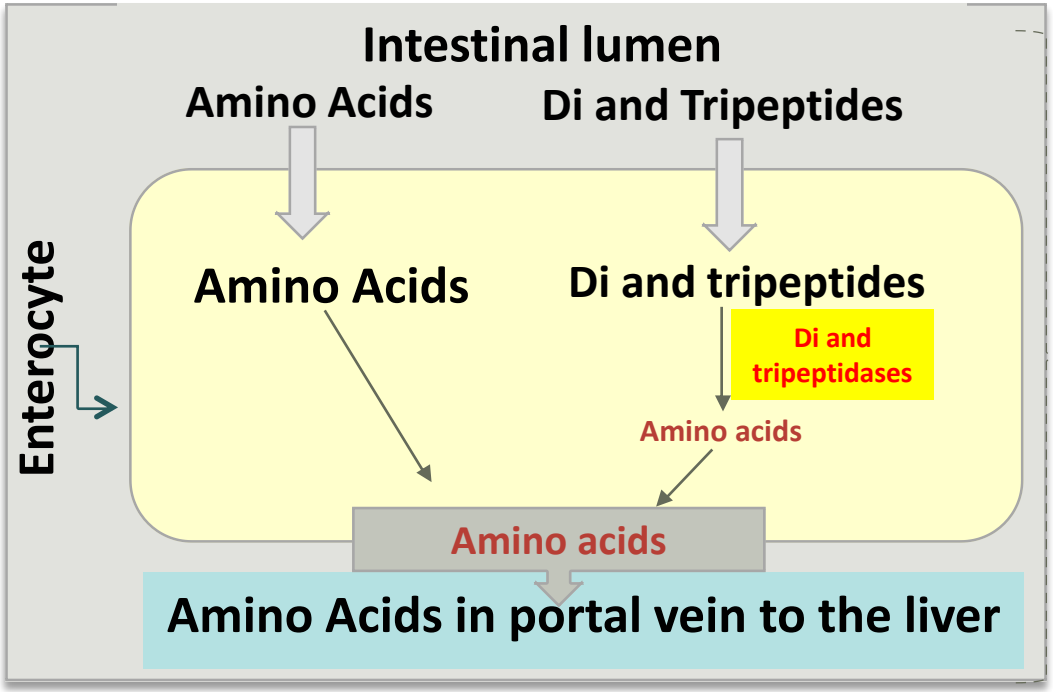
The source of proteolytic enzymes responsible for degrading dietary proteins:

- The stomach
- The small intestine
- The pancreas

Digestion of proteins in Small intestine:

B. digestion by intestinal aminopeptidase..

- **What is Aminopeptidase?** an exopeptidase on the luminal surface of the intestine.
- **Function \ role:** cleaves **Oligopeptides** that result from the action of pancreatic proteases into **free amino acids** and **smaller peptides** (di and tri-peptides).



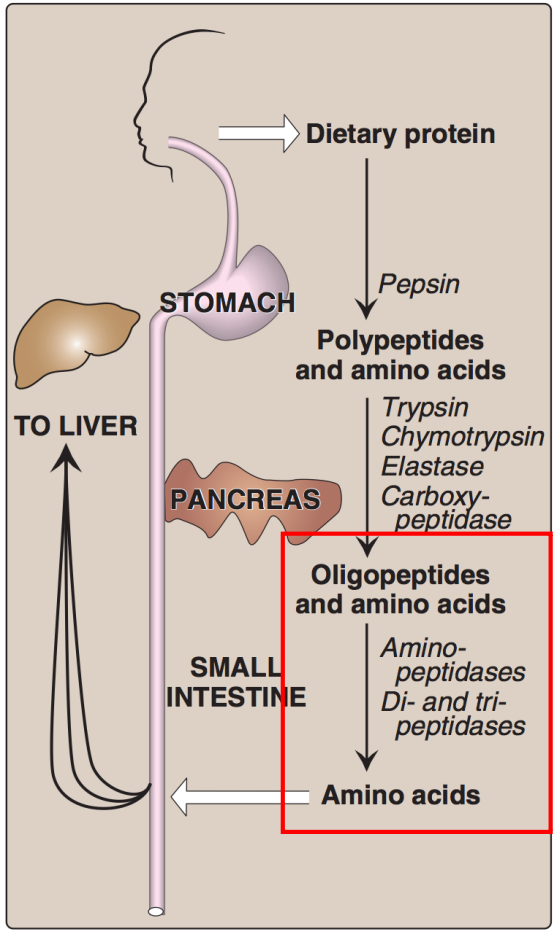
Absorption of digested proteins:

Free amino acids are taken into the enterocytes system sodium-linked secondary transport system.

Di- and tripeptides, however, are taken up by a proton-linked transport system.

The peptides are hydrolyzed in the cytosol to amino acids that are released into the portal system by facilitated diffusion. Therefore, only free amino acids are found in the portal vein after a meal containing protein.

These amino acids are either metabolized by the liver or released into the general circulation.

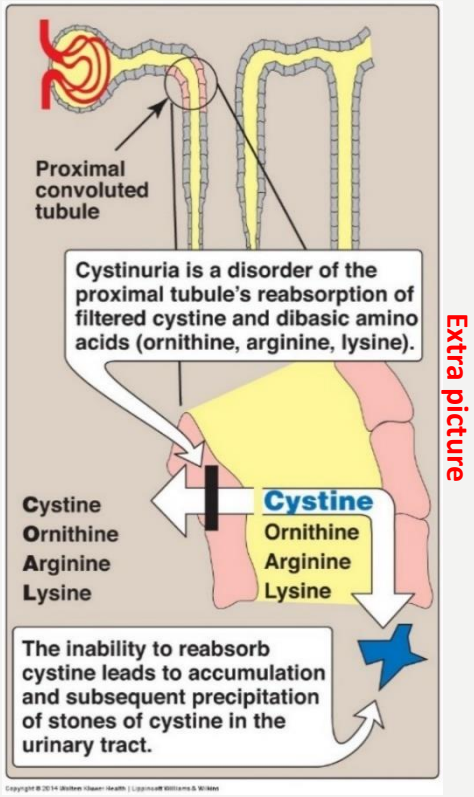


Protein digestion

Genetic errors in amino acids transport

Cystinuria

- one of the most common genetic error of **amino acid transport**.
  - It is an example of inherited disorder in the transport of certain amino acids.
  - It affects the transport of **Cystine** and **dibasic amino acids**.
- **Affected organs:** the **small intestine** and the **kidney.**
- **Urine features:** Cystine and dibasic amino acids appear in the urine.
- **Clinically:** there is kidney stones formation Flank pain , blood in urine.
- **Treatment:** **Oral hydration** (drinking lots of water) is an important part of treatment (to prevent kidney stones formation).



Extra picture

Extra explanation:
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.

You guys have to know the difference between **Cysteine and Cystine** :
- ***Cysteine:*** is a sulfur-containing amino acid.
- ***Cystine:*** is formed from two cysteine molecules joined together

So be carful while choosing your answer, we're talking about the one WITHOUT"E".
د.سمبل مره ركزت على الفرق..الأسماء المتشابهة بالإختيارات لعبة البايوكمستري فركزوا..

Abnormalities of protein digestion

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

→ **In**complete digestion & absorption of **lipids** & proteins

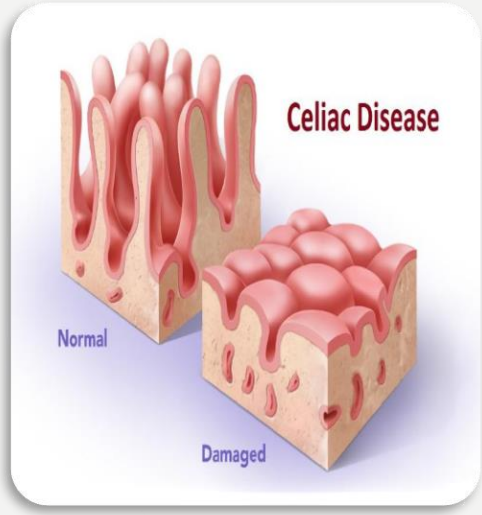
→ abnormal appearance of lipids (steatorrhea) & undigested proteins in the feces

*Steatorrhea is the presence of excess fat in feces.

When the food is not absorbed in the small intestine, it goes to the large intestine, and the bacteria there will act upon the food producing Co2, H+, and metabolites(lactic acid, acetic acid). These metabolites actually lead to absorption of water into lumen leading to diarrhea

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**.
- **Gluten** is a protein found in wheat, rye, and barley. (الحبوب)
- This is an autoimmune disease.



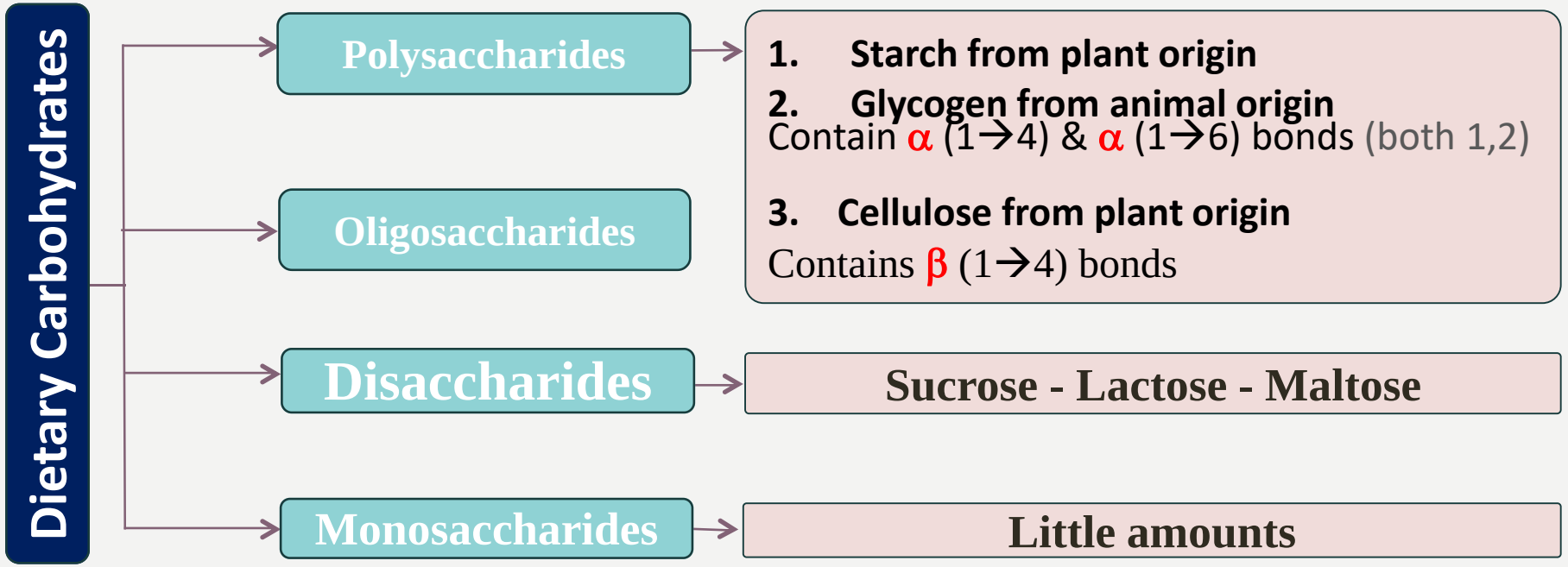
How is it diagnosed?
Gliadin are component of Gluten, it's the molecule that is the epitope for this immune response. There are antibodies used for diagnosis known as "Anti-gliadin Antibodies".

Part II:
Biochemical Aspects of Digestion of carbohydrates:

Carbohydrates digestion

- **Carbohydrates digestion is rapid:**
- Generally completed by the time the gastric contents reach the junction of the duodenum & jejunum.
- **Sites for digestion of dietary carbohydrates:**
  - **The mouth.**
  - **The intestinal lumen.** (mainly the duodenum & jejunum).

Carbohydrate digestion



Enzymes for Digestion of Dietary Carbohydrates

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

Effects of α-amylase on Glycogen

Products	Hydrolysis of
Mixture of short **oligosaccharides** (both branched & unbranched)	α(1,4) glycosidic bonds
Disaccharides: Maltose and isomaltose	

- ✓ **No dietary carbohydrate digestion occurs in the stomach.(why?)**
  - 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 (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.

Measurement

- 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

Enzymes	• **Disaccharidases** and trisacchridases • 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.
Location of their action	• the mucosal lining of the **jejunum**.

Intestinal disaccharidases

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.

If we can't digest cellulose, why do we need it in our body?
It helps in intestinal motility, and Add fibers to the digested food. People who have digestive problems like constipation or diarrhea are suggested to include cellulose in their diet .

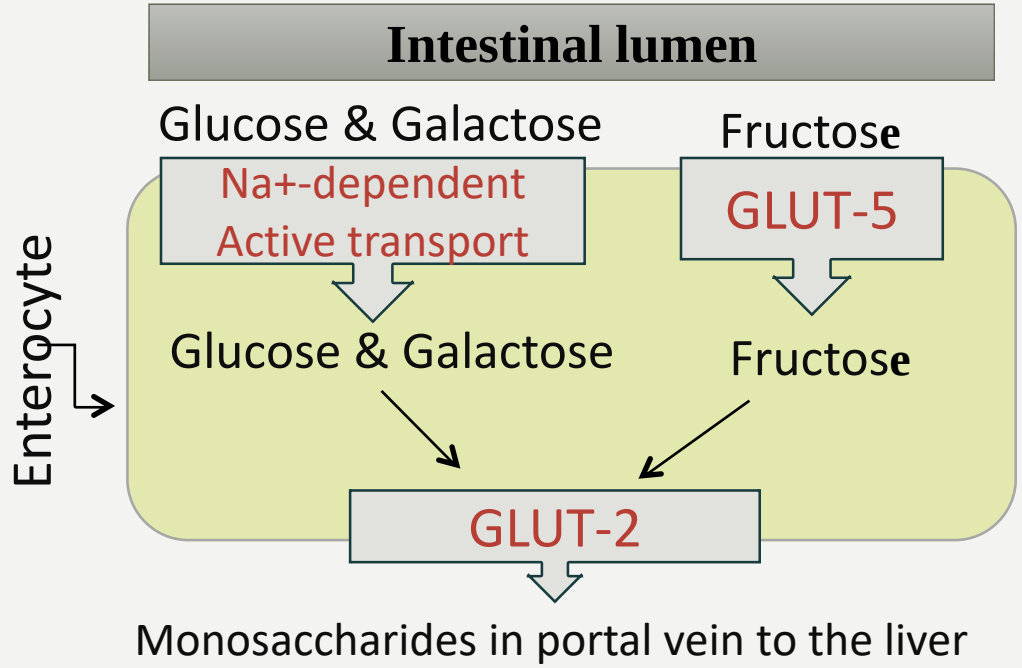
Absorption of Monosaccharaides by Intestinal Mucosal Cells

- **Location:** Duodenum & upper jejunum.
- **Insulin:**

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

- **Different monosaccharides have different mechanisms of absorption:**

1. Facilitated diffusion (GLUT-mediated)
2. Active transport (Energy-dependent): Co-transport with Na+(against the conc.)

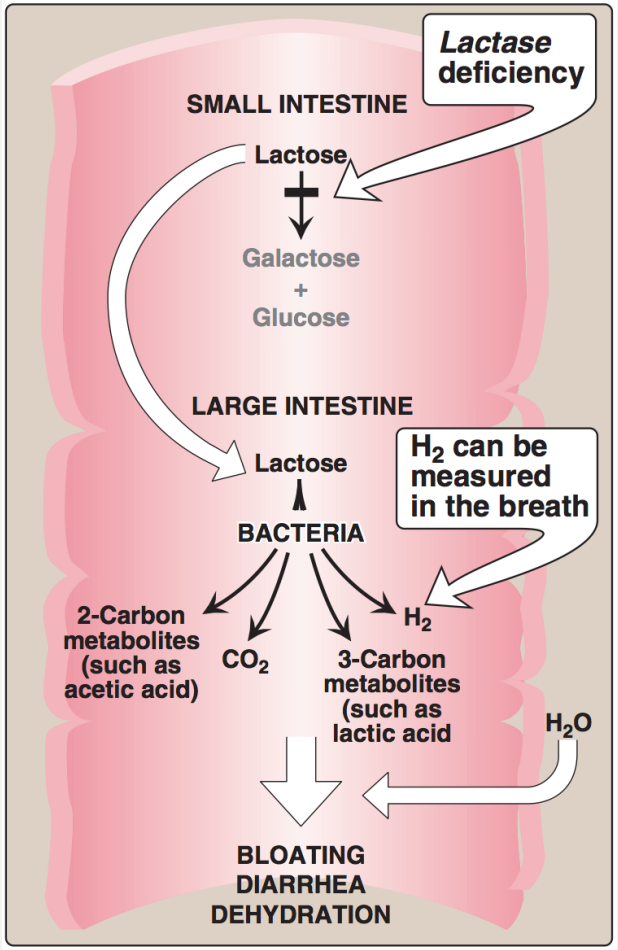


Abnormal digestion of disaccharides (e.g. of lactose)

Lactose intolerance(lactase deficiency)

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

Bacterial fermentation by E. coli of the undigested compounds in the large intestine → CO2, H2 gas → abdominal cramps, diarrhea & distension (flatulence)



-With aging, some people are no longer able to digest milk due to deficiency of lactase. So, lactose goes to large intestine and are acted upon by bacteria. Bacteria will produce metabolites that cause spontaneous movement of water to lumen leading to diarrhea(similar to the explanation in the 10th slide)

-patients have to reduce milk intake, and are suggested to to eat yoghurt or cheese because it has less lactose in it

Check your understanding!

Q1: The gastric secretion for neonates and infants is:

A. Renin.
B. HCL.
C. Pepsin.
D. Pepsinogen.

Q2: Denatured proteins are more susceptible to hydrolysis by:

A. Pepsin.
B. Proteases.
C. HCL.
D. Renin.

Q3: The presence of partially digested proteins and lipids in the upper small intestine stimulates which hormone:

A. Cholecystokinin.
B. Secretin.
C. Gastrin.
D. Motilin.

Q4: Digestion of proteins by pancreatic enzymes result in:

A. Polypeptides.
B. Fatty acid only.
C. Oligopeptides.
D. Amino acid.

Q5: Which one of the pancreatic enzymes activates all of the pancreatic enzymes including itself:

A. Chymotrypsin.
B. Elastase.
C. Trypsin.
D. Carboxypeptidases.

Q6: Incomplete transport & digestion of fat & proteins is a sign of:

A. Stomach insufficiency.
B. Pancreatic insufficiency.
C. Intestinal insufficiency.
D. Spleen disease.

Q7: Steatorrhea indicates which of the following:

A. Presences of proteins in feces.
B. Presences of lipids in feces.
C. Presences of sugar in feces.
D. Presences of fat in feces.

1.A 2.B 3.A 4.C 5.C 6.B 7.D

Check your understanding!

Q8: The rising in α-amylase is due to:

A. Peptic ulcer.
B. Acute pancreatitis.
C. Appendicitis.
D. None of the above.

Q9: Where is the dietary carbohydrates occurs in:

A. Stomach.
B. Mouth.
C. Intestine.
D. All of the above.

Q10: The final digestion of carbohydrates occurs in:

A. Mucosal lining of large intestine.
B. Mucosal lining of stomach.
C. Mucosal lining of small intestine.
D. None of the above.

Q11: Chylomicrons remnants will stay in the bloodstream until they are interact via apolipoptrotein E which are found in:

A. Adipose tissue.
B. Muscles.
C. Blood.
D. Liver.

Q12: The product from action of isomaltase on intestinal disaccharides is:

A. 2 Glucose.
B. 3 Glucose.
C. Glucose & fructose.
D. Glucose & galactose.

8.B 9.A 10.C 11.D 12.A

Done by:

شهد العنزي.–

عبدالله الغزي. –

عاصم الوهيبي. –

جواهر الحربي. –

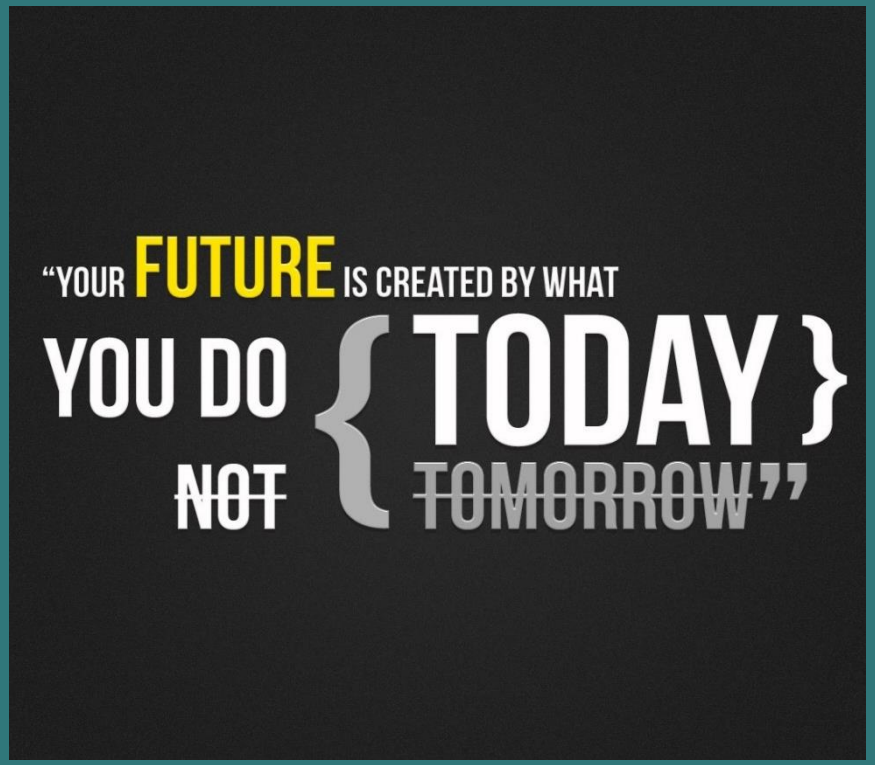
مروج الحربي. –

منيرة الحسيني. –

عبدالله الشنيفي. –

فراس المؤمن. –

أحمد الرويلي. –



Resources:

- 435's slides and notes.
- Lippincott's illustrated reviews: Biochemistry – sixth edition

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