BIOCHEMISTRY OF GI TRACT

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FMUI
Nutrients

CH
Protein
Lipid
Vitamin
Mineral
Water

Digestion

Absorption

Energy

Metabolism
CARBOHYDRATE DIGESTION

Begin in mouth - saliva, contain mucin (glycoprotein) – act as lubricant – promote swallowing of food

Mastication of food → make the surface area of food >> → more available to digestion by digestive enzyme
Salivary amylase (ptialin) – hydrolized $\alpha(1\rightarrow 4)$ glicosidic bond of amylum / glycogen, produced dextrin + maltose + isomaltose

From mouth $\rightarrow$ enter the esophagus $\rightarrow$ stomach – activity of salivary amylase was stopped due to acidity of gastric environment.

In stomach – CH was not digested, but HCl from the stomach promote hydrolysis of glycosidic bond.
In duodenum – pancreas and bile were secreted into the duodenum – the pH of pancreatic juice and bile neutralize the acidic pH of food comes from the stomach.

Pancreatic \( \alpha \)-amylase – hydrolyzed the \( \alpha(1 \rightarrow 4) \)-glycosidic bond – produced maltose + isomaltose + limit dextrin.
In jejunum

- **Disaccharidase** – produced by *brush border* of intestinal mucosal cells
- **Sucrase – isomaltase complex**
  - sucrose $\rightarrow$ fructose + glucose
  - maltose $\rightarrow$ 2 glucose
  - isomaltose $\rightarrow$ 2 glucose
- **Lactase** : lactose $\rightarrow$ galactose + glucose
- **Trehalase** : trehalose $\rightarrow$ 2 glucose
Lactose intolerance

• Lactose intolerance – due to low activity of lactase

• Lactose which is not digested by lactase – was fermented by intestinal microorganism – osmotic active – retain water – symptoms: intestinal cramp, bloated, diarrhea after consuming milk

- primary lactose intolerance
  → common in non Caucasian race

- secondary lactose intolerance
  → caused by enteritis, Kwashiorkor
ABSORPTION OF CH

- Digestion products of CH – glucose, fructose, galactose

- Glucose & galactose – absorbed into intestinal epithelial cells, via
  - $\text{Na}^+$-dependent glucose transporter (SGLT1)
  - facilitated diffusion (GLUT5)

- Fructose – absorbed into intestinal epithelial cells via GLUT 5

- Glucose, fructose, galactose – from intestinal mucosal cells – enter blood vessel through diffusion facilitated by GLUT 2
Figure 1. Absorption of CH
DIGESTION OF LIPID

- **Lingual lipase** hydrolyzed triacylglycerol (TAG), produced → 1,2-diacetylglycerol (1,2-DAG) + fatty acids

- Lingual lipase – hydrolized TAG containing short chain fatty acid (SCT) or medium chain fatty acid (MCT)

- Activity is not inhibited by acidity of the stomach

- Product of digestion SCT / MCT – enter the blood circulation
Figure 2. Structure of triacylglycerol (TAG)
Warm temperature of stomach, peristaltic movement - promote the emulsification of lipid

Lipase produced by the stomach – its activity is not significant – due to inappropriate pH of the stomach

More significant – the activity of lingual lipase - still active in acidic pH of the stomach
In duodenum, TAG was hydrolyzed by pancreatic lipase

- Pancreatic lipase - need colipase for its activity
- Specifically hydrolyzed the ester bond in position 1 & 3 – produced 2-monoacylglycerol (2-MAG) + fatty acid
- 2-MAG was converted into 1-MAG, hydrolyzed into → glicerol + fatty acid
End-products of pancreatic lipase digestion

- 2-MAG (~ 72 %)
- 1-MAG (~ 6 %)
- Glycerol (~ 22 %)
- Fatty acid

Bile – promote digestion and absorption of lipid – by forming micelles – increased solubility of lipid
ABSORPTION OF LIPID

In intestinal epithelial cells

• 2-MAG, 1-MAG, fatty acids were reconverted into TAG - transported in lymph vessel – packed as chylomicron – enter the blood circulation

• Glycerol – directly enter the portal vein – to the liver
Figure 3. Absorption of lipid (resynthesis of TAG)
DIGESTION OF PROTEIN

• Digestion of protein was begun in the stomach

• **HCl** in the stomach
  - denature the protein
  - synthesized by parietal cells
  - its synthesis need energy

• **Pepsin** – produced by *chief cells* – was secreted as inactive precursor – pepsinogen

• Activation of pepsinogen – was carried by HCl and by pepsin itself (*autocatalysis*)
Figure 4. Synthesis of HCL

Parietal cell of the stomach

Plasma

Lumen of the stomach

CO$_2$ → CO$_2$ → H$_2$CO$_3$ → H$_2$O

HCO$_3^-$

Cl$^-$

K$^+$ → H$^+$

HCl

Cl$^-$
• Pepsin – is an endopeptidase

• Hydrolyzed peptide bond intramolecule of protein, near the C-end of aromatic amino acid residue or acidic amino acid residue

• End-product digestion of pepsin – small peptides, contain no free amino acid
In the stomach – rennin enzyme – important for digestion of protein in infant

Converted casein into paracasein, which was hydrolyzed further by pepsin

\[
\text{Casein} \xrightarrow{\text{rennin}} \text{paracasein} \xrightarrow{\text{pepsin}} \text{peptide}
\]
Pancreatic juice contain proteases

- Tripsinogen
- Chymotripsinogen
- Proelastase
- Procarboxyypeptidase

Tripsinogen was activated by enteropeptidase (produced by duodenal epithelial cells)

Tripsin activate chymotripsinogen, proelastase, procarboxyypeptidase
• Tripsin – cleaved the peptide bond near the C-end of Lys or Arg residue
• Chymotripsin - cleaved the peptide bond near the C-end of hydrophobic or acidic residue of amino acid
• Elastase – cleaved the peptide bond near the Ala, Gly or Ser residue

Tripsin, chymotripsin, elastase – are endopeptidase

Carboxypeptidase – is an exopeptidase – cleaved the peptide bond near the C-terminal end of polypeptide – produced free amino acid
Intestinal mucosal cells – produced **aminopeptidase**

End-product digestion of protein
- amino acid
- tripeptide
- dipeptide

Tripeptide, dipeptide, intra mucosal cells will be hydrolyzed by **tripeptidase, dipeptidase** – produced **amino acid**
Amino acids were absorbed from intestinal lumen into intestinal epithelial cells via

- **Na\(^+\)-dependent** active transport
  - need **energy**
  - specific **protein carrier** – for certain amino acid

- **γ-glutamil cycle**
  - amino acid react with glutathione (γ- glutamil-sisteinil-glisin)
  - γ-glutamil-amino acid across the membrane – liberate into cells

- **Diffusion** – from epithelial cells – enter the blood circulation
Figure 5. Absorption of amino acid
PUTREFACTION

• Food – which were not digested or absorbed – were moved by peristaltic movement – enter the colon

• In the colon – water was reabsorbed – the consistency of colon content become more solid gradually

• Also occurred the putrefaction and fermentation by the microorganism in the colon

• Microorganism in the colon - ± 25 % fecal weight – role in synthesis of vitamin K & vitamin B12
Product of putrefaction
- Lactic acid, acetic acid, propionic acid, butyric acid
- CO2, methane, H2, N2, H2S
- Toxic substances containing-N
  - ptomaine (toxic amine)
  - ammonia
- Indol & skatol – putrefaction product of tryptophane – characteristic odor of feces
- Ethyl mercaptan, methyl mercaptan – putrefaction product of cysteine
• **Ammonia / toxic amine** – were absorbed along with water – enter the liver – detoxified in the liver – were converted into **urea** (not toxic) – excreted through the kidney – via urine

• In liver disease – detoxifying function of liver ↓ - blood ammonia ↑ - toxic – especially for nerve tissue – **coma hepaticum**

• To prevent coma hepaticum
  - administration of neomicyn (antibiotic) – killed the intestinal bacteria – production of ammonia ↓ - blood ammonia ↓
  - low protein diet
FIBER

• Cellulose, hemicellulose, pectin, lignin

• CH which were COULD NOT digested or absorbed by human

• Important in the diet

∀ ↑ the volume of GI tr content – hygroscopic – promote defecation

∀ ↓ the absorption of cholesterol – to prevent hypercholesterolemia & atherosclerosis

∀ ↑ fiber dietserat – ↓ incidence of Ca colon
BILE
• Bile was produced in the liver – stored in gall bladder – secreted into the duodenum in response to stimulation of food containing fat

• Contain – bile acid, bile pigment, cholesterol, fatty acid, inorganic salts

• Function
  - fat emulsification – promote digestion and absorption of fat + vitamin A, D, E, K
  - neutralize acid
  - excretion for bile acid, bile pigment empedu, cholesterol, toxin, drugs
  - cholesterol solubility
PORPHYRIN & BILE PIGMENT METABOLISM
PORPHYRIN

- Cyclic compound – formed by 4 pyrole ring – linked by methenyl bridge

- Can form complex with
  - Fe → produced heme (nonprotein part of hemoglobin / myoglobin)
  - Mg → produced chlorophyll plant pigment, light energy acceptor in photosynthesis

- Compounds which contain porphyrin
  - Hemoglobin
  - Myoglobin
  - Cytochrome
  - Catalase
BIOSYNTHESIS of PORPHYRIN

• First step:
  Glycine + succynil CoA → δ-amino levulinate (ALA)
  - catalyzed by ALA synthase, need pyridoxal phosphate
  - regulation step for synthesis of porphyrin, through
    - Feed back inhibition by heme
    - Repression of synthesis ALA sintase – at the gen level

• Final step:
  Incorporation of Fe into the porphyrin ring, catalyzed by heme synthase atau ferochelatase
Figure 6. Biosynthesis of porphyrin / heme

Succynil CoA + glycine
- ALA synthase, piridoxal-P

ALA

Porphobilinogen

Uroporphyrinogen III

Coproporphyrinogen III

Protoporphyrinogen III

Protoporphyrin III

Fe

Hem

Protein

Hb, Mb, Cyt, catalase
CATABOLISM of HEME – Production of bile pigment

• Life span of erythrocyte - 120 days

• Senescence erythrocytes – were removed from circulation – degraded in the RES / spleen

• 1 g Hb – produced ± 35 mg bilirubin

• Bilirubin formation in human adult - ± 350 mg / day
Figure 7. Catabolism of Heme
Figure 8. Structure of heme & bile pigment
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Figure 9. Catabolism of heme into bile pigment
BILE ACID / SALT

• Synthesized from cholesterol in the liver through hydroxylation, reduction, oxidation

• Conjugation with glycine & taurine – forming glycholate & glycochenocholate, taurocholate & taurochenocholate – primary bile acid / salt

• Secreted into bile

• Stored in the gall bladder

• Deliver to the intestine – in response to stimulation of food containing fat

• Act as detergent – promote digestion of fat
• In intestine – primary bile acid undergoes deconjugation and dehydroxylation – forming **secondary bile acid** – deoxycholic acid & lithocholic acid

• In ileum – > 95 % secondary bile acid were absorbed – transported to the liver through **enterohepatic circulation** – resecreted into the bile

• < 5 % - were excreted in the feces

• **Excretion of bile acid** in the feces – is the main route for excretion of cholesterol
Figure 10. Structure of bile acids
Figure 11. Enterohepatic circulation of bile acid/salt

Liver (synthesizes 0.2–0.6 g/day and recycles >95%) Secondary bile salts are reconjugated

Bile salts reabsorbed (12–32 g/day) and returned to liver for recycling > 95% efficiency

Pool of bile salts = 2–4 g (recycles 6–8 times/day) Bacteria in gut deconjugate and dehydroxylate bile salts

< 5%

Feces (0.2–0.6 g/day)
XENOBIOTIC METABOLISM
Human
• Every moment exposed to various chemical substances (xenobiotics)
• Drugs, food additives, pollutants, cosmetics

Knowledge in xenobiotic – important to understanding the
• Pharmacology
• Toxicology
• Cancer
• Drug addiction

Xenobiotic metabolism – 2 phase
Xenobiotic metabolism – once was known as detoxication reaction – NOT fully appropriate – because sometimes the substances become more toxic

More appropriate – biotransformation reaction
Reaction of phase I of xenobiotic metabolism
Hydroxylation by cytochrome P450 / monooxygenase

\[ \text{RH} + \text{O}_2 \rightarrow \text{R-OH} + \text{H}_2\text{O} \]

Cyt P450 (CYP450)
- Hemoprotein
- Present in reticulum endoplasmic membrane
- Need NADPH as coenzyme (from HMP shunt)
- Also play role in biosynthesis of fatty acid & cholesterol
Reaction of phase II of xenobiotic metabolism - conjugation with endogenous substances

- Glucuronic acid
- Sulfate
- Acetate
- Glutathione (GSH)
- Amino acids
- Methyl group

Purpose of reaction of phase I & phase II – ↑ solubility & polarity of xenobiotics (lipophilic → hydrophilic) – easy to be excreted
Figure 12. Biotransformation reaction of xenobiotic
Terima Kasih