Micronutrients: Digestion & Absorption

VITAMIN A

• Digestion & Absorption
  • Absorbed primarily by jejunum & ileum.
  • Retinol is found typically bound to fatty acid esters (most common retinyl palmitate).
  • Retinyl esters and beta-carotene are often bound to protein in food from which they must be released.
  • Hydrolysis from protein occurs by the action of pepsin in the stomach and other proteolytic enzymes in the proximal SI (heating of plant food before consumption is thought to facilitate bioavailability by weakening protein-carotenoid complexes).
  • Hydrolysis of retinyl and carotenoid esters by various esterases occurs at the same time fats, phospholipids are being hydrolyzed by pancreatic enzymes.
  • Following hydrolysis, retinol is taken up by the enterocytes. The hydrolysis of retinyl esters requires the presence of bile salts that serve to solubilize them in mixed micelles.

VITAMIN D

• Digestion & Absorption
  • About 50% of dietary vitamin D is absorbed.
  • The rate of absorption is most rapid in the duodenum, but the largest amount is absorbed in the terminal ileum.
  • Vitamin D from the diet is absorbed from a micelle, in association with fat and with the aid of bile salts, by passive diffusion into the intestinal cell.

VITAMIN E

• Digestion & Absorption
  • Tocopherols are absorbed by jejunum & tocotrienols are absorbed by the terminal ileum.
  • Tocopherols are found free in foods; tocotrienols are often esterified, requiring pancreatic esterase and/or duodenal mucosal esterase that function at the brush border of the intestine to hydrolyze tocotrienols for absorption.
  • Free tocopherol is absorbed, as part of micelles, by passive diffusion.
  • Bile and pancreatic juices required for micelle formation.
  • Simultaneous digestion and absorption of dietary lipids, including medium-chain triacylglycerols with vitamin E improves absorption of vitamin E.
  • Absorption varies from 20% to 50% absorption and may be as high as 80%. As vitamin E intake increases, vitamin E absorption decreases.

VITAMIN K

• Digestion & Absorption
  • Phylloquinone is absorbed in the SI (jejunum) by a saturable energy-dependent process.
• Other forms (menaquinones and menadione) are absorbed by passive diffusion in the terminal ileum and colon.
• Bile and pancreatic secretions enhance absorption (just like other fat-soluble vitamins).
• Absorption varies: 40-80% absorbed (20-30% if fat malabsorption) of dietary vitamin K.
• A number of bacterial species can synthesize menaquinones – it is unclear how much can be absorbed.

### Thiamin (Vitamin B1)

#### Digestion & Absorption
- In plants, thiamin exists in its free form. In animal foods, > 95% occurs in a phosphorylated form (primarily as Thiamin Diphosphate (TDP) and Thiamin Triphosphate (TPP)).
- Intestinal phosphatases and pyrophosphatases remove the phosphate prior to absorption.
- Absorption (free thiamin, not phosphorylated thiamin) can be both active and passive, depending on the amount present in the intestine.
- If in small amounts, there is a sodium-dependent, active, saturable transport mechanism in the upper jejunum, but can occur in duodenum and ileum. If in larger amounts, passive diffusion.
- Ethanol ingestion interferes with the active transport.

### Riboflavin (Vitamin B2)

#### Digestion & Absorption
- The form of riboflavin in food varies. In some foods riboflavin is found as free or protein-bound riboflavin. In other foods riboflavin is found as Flavin Mononucleotide (FMN) or Flavin Adenine Dinucleotide (FAD).
- Need to remove protein and phosphate (phosphatases) to absorb. Riboflavin attached to protein is freed by the action of HCL and gastric and intestinal enzymes.
- Riboflavin in food as FMN and FAD must be freed prior to absorption. Within the intestinal lumen, enzymes such as FAD pyrophosphatase and FMN phosphatase play an important role.
- Animal sources of riboflavin are thought to be better absorbed than plant sources.
- Better absorbed with meals (70% absorption) than fasting (15%).
- Divalent metals (Copper, Zinc, Iron, Manganese) may chelate riboflavin and inhibit absorption.
- Free riboflavin is absorbed by active transport (sodium-dependent), mainly in the duodenum.
- A small amount of riboflavin is absorbed in the large intestine.

### Niacin (Vitamin B3)

#### Digestion & Absorption
- Nicotinamide Adenine Dinucleotide (NAD) and Nictinamide Adenine Dinucleotide Phosphate (NADP) may be hydrolyzed within the intestinal tract by glycohydrolase to free nicotinamide.
- Nicotinaminde and nicotinic acid can be absorbed in stomach, but more readily in small intestine.
- Once in the intestinal cell, nicotinic acid is believed to be converted into nicotinamide.

### Pantothentic Acid (Vitamin B5)

#### Digestion & Absorption
- CoA is hydrolyzed in small intestine to pantotheine and then to pantothentic acid; free pantothentic acid absorbed by saturable sodium-dependent active process.
- About 40-60% of the ingested pantothentic acid is absorbed, less (10%) if taken in larger amounts (10 times the recommended amount).
- Panthenol (alcohol form of the vitamin) may be absorbed and converted to pantothenate.
- Within cells, pantothentic acid is metabolized to CoA. CoA is used for the synthesis of ACP (acyl carrier protein) of the fatty acid synthase enzyme, which catalyzes fatty acid synthesis.
Pyridoxine (Vitamin B6)

- Digestion & Absorption
  - For absorption, the phosphorylated forms need to be dephosphorylated.
  - AP (alkaline phosphatase) found at the brush borer of the intestine hydrolyze the phosphate → yield either pyridoxine (PN), pyridoxal (PL), or pyridoxamine (PM).
  - Absorb about 70-80% depending on glycosides (more poorly absorbed) by passive diffusion in jejunum.
  - Some PN glucoside is absorbed intact and the complex will be excreted unchanged in the urine.
    - In an average U.S. diet, absorption of PN-glucosides range from 71% to 85%.
  - In enterocytes they are (all forms) rephosphorylated (by kinases) and most is converted to pyridoxal phosphate (PLP).

Folate (Vitamin B9)

- Digestion & Absorption
  - Natural folate is delivered by food in bound form which is combined with a string of amino acids known as polyglutamates (up to 9 glutamate), which are hydrolyzed at the brush border membrane to monoglutamate, by the γ-glutamylcarboxypeptidases (also called conjugases), which are zinc dependent. The conjugases are also found in the pancreatic juice, and bile.
  - The intestine absorbs this folate form with only one monoglutamate attached. Absorption is via a saturable active transport, carrier-mediated, sodium-dependent channel, mainly in the jejunum. Optimal transport occurs between a PH of 5 & 6.
  - Folate needs vitamin B12 to function. Vitamin B12 acts to remove a methyl group (CH3) from tetrahydrofolate. If this does not occur, folate will become trapped in cells in its methyl form leaving it unavailable to support DNA synthesis and cell growth.

Cobalamin (Vitamin B12)

- Digestion & Absorption
  - Absorption of vitamin B-12 from food requires normal function of the stomach, pancreas, and terminal ileum. Vitamin B-12 in food is bound to protein and is released in the stomach by the acid environment and proteolytic enzyme pepsin.
  - Stomach acid and enzymes free vitamin B-12 from food, allowing it to bind to other proteins, known as R proteins.
  - R proteins are degraded by pancreatic enzymes, freeing vitamin B-12 to bind to intrinsic factor (IF), a protein secreted by the parietal cells in stomach.
  - The IF-B-12 complex binds to the IF receptor (on the surface of the SI) in the presence of calcium, and the complex is internalized by a receptor-mediated endocytotic process. The IF is degraded and the B-12 is released into the cytosol.

Biotin

- Digestion & Absorption
  - Biotin is found bound to protein or as biocytin (also called biotinyllysine [contains lysine and is a biologically active derivative]).
  - Avidin is a glycoprotein found in egg white, which binds biotin and prevents its absorption.
    - Cooking egg white denatures avidin, rendering it susceptible to digestion, and unable to prevent the absorption of dietary biotin.

Vitamin C (Ascorbate)

- Digestion & Absorption
  - In men and guinea pigs: vitamin C absorbed in ileum by active transport mechanism (sodium-dependent, energy requiring, carrier mediated transport system).
  - Losses of up to 20% occur during absorption (destroyed in GI tract).
  - Prior to absorption, ascorbate may be oxidized to dehydroascorbate (DHAA, absorbed by passive diffusion). Vitamin C crosses the cell membranes in the form of DHAA.
• Pectin (14.2 g/day) (mechanism unknown) and zinc (9.3 mg/day) may impair the absorption of vitamin C.

• In the GI tract, a high iron concentration present with vitamin C results in the oxidative destruction of vitamin C yielding → 2,3-diketogulonic acid (no vitamin C activity).

**CALCIUM**

- **Factors that Enhance Absorption**
  - Vitamin D enhances calcium absorption. 1,25-Dihydroxyvitamin D, the major metabolite, stimulates active transport of calcium in the small intestine and colon.
    - Deficiency of 1,25-dihydroxyvitamin D, caused by inadequate dietary vitamin D, inadequate exposure to sunlight, impaired activation of vitamin D, or acquired resistance to vitamin D, results in reduced calcium absorption.
  - Lactose appears to improve calcium absorption possible by improving solubility (more pronounced in infants than adults).

- **Factors that Inhibit Absorption**
  - Oxalic acid, also known as oxalate, is the most potent inhibitor of calcium absorption (may chelate calcium and increase fecal excretion of the complex), and is found in high concentrations in spinach, rhubarb, Swiss chard, and beetroot; moderate concentration in peanuts, okra, eggplant, and squash; and somewhat lower concentrations in sweet potato and dried beans.
  - Phytic acid is a less potent inhibitor of calcium absorption than oxalic acid. Yeast possess an enzyme (phytase) which breaks down phytic acid in grains during fermentation, lowering the phytic acid content of breads and other fermented foods. Only concentrated sources of phytate such as wheat bran or dried beans substantially reduce calcium absorption.
  - Fiber may decrease calcium absorption. Nonfermentable fiber (cellulose or those found in wheat bran) can increase bulk and decrease transit time → decreasing the time available for calcium absorption.
  - Caffeine: Caffeine in large amounts increases urinary calcium for a short time. On average, one 8-ounce cup of coffee decreases calcium retention by only 2-3 mg. One observational study found accelerated bone loss in postmenopausal women who consumed less than 744 mg of calcium per day and reported that they drank 2-3 cups of coffee per day.
  - Magnesium and calcium compete with each other for intestinal absorption whenever an excess of either is present in the GI tract.
  - Sodium: Increased sodium intake results in increased loss of calcium in the urine, possibly due to competition between sodium and calcium for reabsorption in the kidney. Each 2.3 gram increment of sodium (6 grams of salt; NaCl) excreted by the kidney has been found to draw about 24-40 mg of calcium into the urine. In adult women, each extra gram of sodium consumed per day is projected to produce an additional rate of bone loss of 1% per year if all of the calcium loss comes from the skeleton.
  - Phosphorus: A dietary calcium:phosphorus ratio of 1:1 is recommended. Diets high in phosphorus and low in calcium (4:1 ratio) have been found to increase parathyroid hormone secretion (secondary hyperparathyroidism). The substitution of large quantities of soft drinks for milk or other sources of dietary calcium is cause for concern with respect to bone health in adolescents and adults.
  - Fat malabsorption (steatorrhea > 7g of fecal fat/day) can interfere with calcium absorption through the formation of insoluble soaps (Ca-FA complex) in the lumen of the SI. These calcium soaps can be absorbed and are excreted in the feces.
  - Protein: As dietary protein intake increases, the urinary excretion of calcium also increases. Because only 30% of dietary calcium is generally absorbed, each one-gram increase in protein intake/day would require an additional 5.8 mg of calcium/day to offset the calcium loss.

**PHOSPHORUS**

- **Digestion & Absorption**
Phosphorous in food exists as inorganic and organic forms (e.g. phosphoproteins, phospholipids).
Most phosphorous is absorbed in its inorganic form – there are phosphatases in the lumen of the SI.
About 50-70% of phosphorous is absorbed with normal intake, and up to 90% when intake is low.
We don’t know if active transport or diffusion
Vitamin D (calcitriol) increases absorption, and dietary calcium, magnesium, and aluminum reduce absorption.

**Potassium**

- **Digestion & Absorption**
  - Readily absorbed (> 90%) in small intestine and colon
  - It is believed that K⁺ may be absorbed through the apical membrane of the colonic mucosal cell by a K⁺/H⁺-ATPase pump.

**Sodium/Chloride**

- **Digestion & Absorption**
  - About 95% of ingested sodium is absorbed with the remaining 5% excreted in the feces.
  - 3 pathways for absorption:
    - Na⁺/glucose cotransport system: absorbed rapidly in SI mainly by active transport.
    - Electroneutral Na⁺ and Cl⁻ cotransport system is active in both the SI and the proximal portion of the colon.
    - Electrogenic sodium absorption mechanism is active in the colon. Sodium enters the luminal membrane via a Na⁺ channel.
    - *It is important to recognize that the main driving force for all these pathways is the basolateral Na⁺ pump – i.e. pumping sodium out of the enterocyte.*

**Magnesium**

- **Digestion & Absorption**
  - Generally 30-65% of magnesium is thought to be absorbed in adult with normal intake.
  - Absorption mainly in jejunum and ileum
  - Magnesium absorption is more efficient when magnesiium status is poor or marginal and /or when magnesium intake is low.
    - 65% of Mg is absorbed with an intake of 36 mg versus only 11% absorption with an intake of 973 mg.
  - Two systems - carrier mediated at low concentrations; and simple diffusion at higher concentrations.
- **Nutrient Interactions**
  - Zinc: High doses of zinc in supplement (142 mg/day) in healthy adult males significantly decreased magnesium absorption.
  - Fiber: Large increases in the intake of dietary fiber have been found to decrease magnesium utilization in experimental studies.
  - Protein: Dietary protein may affect magnesium absorption. One study found that magnesium absorption was lower when protein intake was less than 30 grams/day, and higher protein intakes (93 grams/day vs. 42 grams/day) were associated with improved magnesium absorption in adolescents.
  - Vitamin D and calcium: The active form of vitamin D (calcitriol) may increase the intestinal absorption of magnesium to a small extent.
  - Inadequate blood magnesium levels are known to result in low blood calcium levels, and resistance to parathyroid hormone.
  - Unabsorbed fatty acids present in high quantities, as occur with steatorrhea, may bind to magnesium to form soaps. These Mg-FA soaps are excreted in the feces.
• **Digestion & Absorption**

  **Heme Iron**
  - Heme iron is hydrolyzed from the globin part of hemoglobin and myoglobin by proteases from stomach and SI → heme iron is released.
  - Heme iron is absorbed intact as a metalloporphyrin into the mucosal cell of the SI.
  - The proportion of heme iron absorbed depends mainly on iron status, usually 15-35% in persons who are iron-deficient.
  - Iron absorption occur throughout the SI but more efficient in duodenum.

  **Non-heme Iron**
  - Non-heme iron is also usually bound to protein or other food components and must be enzymatically liberated by gastric secretions such as protease and HCl (HCl and pepsin aid in the release of nonheme iron from food component).
  - Once released from food, most nonheme iron is present as ferric (Fe +3) iron in the stomach.
  - In the acidic environment of the stomach, much of the ferric iron may be reduced to the ferrous state. As ferrous move to the alkaline environment in the SI, some ferrous iron may be oxidized to become ferric iron.
  - Ferric iron may further complex to produce Fe(OH)3
    - Ferric hydroxide is relatively insoluble and tends to precipitate → less iron available for absorption.
  - Ferrous iron is absorbed much better than ferric iron – there are specific receptors on the enterocyte for ferrous iron (a membrane protein known as integrin is thought to facilitate iron absorption at the brush border of the enterocyte).
  - Mechanisms of absorption of ferric iron are not well understood, but chelation by ligands is thought to be involved.
  - It is free iron, not chelated iron, that is absorbed into the enterocyte.

  **Factors that Enhance Non-heme Iron Absorption**
  - **Vitamin C**: Vitamin C strongly enhances the absorption of nonheme iron by reducing dietary ferric iron (Fe\(^{3+}\)) to ferrous iron (Fe\(^{2+}\)) and forming an absorbable iron-ascorbic acid complex.
  - Other organic acids: Citric, malic, and lactic acids have some enhancing effects on nonheme iron absorption.
  - Meat, fish, and poultry (MFP): Aside from providing highly absorbable heme iron, meat, fish, and poultry also enhance nonheme iron absorption. The mechanism for this enhancement of nonheme iron absorption is not clear.

  **Factors that Inhibit Non-heme Iron Absorption**
  - Phytic acid (phytate): Phytic acid is present in legumes, grains, and rice and is an inhibitor of nonheme iron absorption.
    - Small amounts of phytic acid (5 to 10 mg) can reduce nonheme iron absorption by 50%. The absorption of iron from legumes, such as soybeans, black beans, lentils, and split peas, has been shown to be as low as 2%.
    - Polyphenols, found in some fruits, vegetables, coffee, tea, wines, and spices, can markedly inhibit the absorption of nonheme iron.
    - Soy protein, such as that found in tofu, has an inhibitory effect on iron absorption that is independent of its phytic acid content.

**Zinc**

• **Digestion & Absorption**
  - The main site of absorption is the proximal SI (jejunum). Absorption varies from 12% to 59%.
  - Zinc needs gastric acid and proteases (also nucleases) to hydrolyze zinc from attachment to proteins and nucleic acids.
- Absorption into the enterocyte is by a carrier-mediated process (the need of energy is unclear) with lower intake and some simple diffusion with higher intake.
- Passive diffusion and paracellular zinc absorption are thought to occur with high zinc intake.

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<th>IODINE</th>
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<td><strong>Digestion &amp; Absorption</strong></td>
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<td>Iodide is absorbed rapidly and completely throughout the GI tract, including the stomach.</td>
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<td>Dietary iodine (I) is either bound to amino acids or is found free, primarily in the form of iodate (IO&lt;sub&gt;3&lt;/sub&gt;−) or iodide (I&lt;sup&gt;−&lt;/sup&gt;).</td>
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<td>During digestion, iodate (from breads) is reduced to iodide by glutathione.</td>
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<td><strong>Digestion &amp; Absorption</strong></td>
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<tr>
<td>Both inorganic and organic forms of selenium are all efficiently absorbed primarily in the duodenum (duodenum &gt; jejunum and ileum &gt; stomach).</td>
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<td>Vitamins C, A, and E enhance selenium absorption.</td>
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<td>Mercury and phytates are thought to inhibit selenium absorption through chelation and precipitation.</td>
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<td>Dietary selenium in the inorganic form such as selenite leads to greater incorporation of the mineral into glutathione peroxidase than when selenomethionine, the organic form, is the dietary form.</td>
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<tr>
<td>Mainly absorbed in the duodenum and rest of small intestine, but some in the stomach. There is a saturable, energy-dependant system and (low amounts) and a nonsaturable passive diffusion system.</td>
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<td>Usually bound to amino acids in proteins of foods so need HCl and pepsin to release copper in the stomach. Other proteolic enzymes may hydrolyze protein and release copper in SI.</td>
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<td>Copper absorption enhanced by some amino acids (especially histidine and sulfur amino acids), organic acids such as citric acid, and low body stores.</td>
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<td>About 30-50% usually absorbed</td>
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