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Food-drug interactions

Dr. Abdalkareem Maghmomeh
Faculty of Pharmacy- Hama University

Definition of Terms

Drug-food interaction: the result of the action between a drug and food that would not happen with the food or the drug alone

Definition of Terms

- **Drug- food interaction:** the result of the action between a drug and a food that would not happen with the nutrient or the drug alone
- **Food-drug interaction:** a broad term that includes drug-food interactions and the effect of a medication on nutritional status

Drug - Food Interaction

- For example, a drug that causes chronic nausea or mouth pain may result in poor intake and weight loss



Key Terms

- **Bioavailability:** degree to which a drug or other substance reaches the circulation and becomes available to the target organ or tissue
- **Half-life:** amount of time it takes for the blood concentration of a drug to decrease by one half of its steady state level
- **Side effect:** adverse effect/reaction or any undesirable effect of a drug

Other Terms

- Bioavailability: % free to function
- Absorption rate: % absorbed and time for absorption
- Transported: amount in blood (free or bound)
- Metabolized: altered by enzymes in tissues
- Mixed-function oxidase system (MFOS): enzyme system that metabolizes drugs and compounds in foods.

Pharmacokinetics

Movement of drugs through the body by

- **Absorption**
- **Distribution**
- **Metabolism**
- **Excretion**

Absorption

- Movement of the drug from the site of administration to the bloodstream; depends on
 - The route of administration
 - The chemistry of the drug and its ability to cross membranes
 - The rate of gastric emptying (for oral drugs) and GI movement
 - The quality of the product formulation
- Food components and nutritional supplements can interfere with absorption, **especially** if the drug is **taken orally**

Distribution

When the drug leaves the systemic circulation and moves to different parts of the body

- Drugs in the bloodstream are often bound to plasma proteins; only unbound drugs can leave the blood and affect target organs
- Low serum albumin can increase availability of drugs and their effects

Metabolism (biotransformation)

- **Primarily in the liver**; cytochrome P-450 enzyme system facilitates drug metabolism; metabolism generally changes fat soluble compounds to water soluble compounds that can be excreted
- Foods or dietary supplements that **increase or inhibit** these enzyme systems can change the rate or extent of drug metabolism

Excretion

- Drugs are eliminated from the body as an unchanged drug or metabolite
 - **Renal excretion** the major route of elimination; affected by renal function and urinary pH
 - Some drugs eliminated in **bile and other body fluids**

Pharmacodynamics

- Physiologic and biochemical effects of a drug or combination of drugs
- The mechanism of action, e.g. **how a drug works**
- Often the drug molecule binds to a receptor, enzyme, or ion channel, producing a physiological response

Factors Affecting the Extent of Interaction Between Foods and Medications

- The dosage of the drug.
- A person's age, size, and state of health.
- When the food is eaten and when the medication is taken.

Classification of Food-Drug Interactions

- 1- **Drugs** can alter **food** intake and affect the absorption, metabolism, and excretion of nutrients.
- 2- Components of **foods** can similarly affect the absorption, metabolism, and excretion of **drugs**.

1- Drug Effects on Food Intake

2- Drug Effects on Nutrient Absorption

3- Drugs Interacting & Altering Metabolism of Nutrients

4- Drug Effects on Nutrient Excretion

Effect of drug on food

1- Drug Effects on Food Intake

Some drugs can make food intake difficult or unpleasant.

Certain side effects, including **abdominal discomfort**, **constipation**, and **diarrhea**

Medications that cause **drowsiness**, can make a person too tired to eat.

Drugs May Alter Food Intake by:

- 1- Altering the appetite (**amphetamines** suppress appetite; **corticosteroids** increase appetite).
- 2- Interfering with taste or smell (**amphetamines** change taste).
- 3- Inducing nausea or vomiting (**digitalis**).
- 4- Interfering with oral function (some **antidepressants** may cause dry mouth).
- 5- Causing inflammation in the mouth (**methotrexate** may cause painful mouth ulcers).

2- Drug Effects on Nutrient Absorption

- **Altered Stomach Acidity:** drugs that reduce stomach acidity as **anti-acid, antiulcer drugs** (such as **proton pump inhibitors** and **H2 blockers**), may interfere with iron and folate absorption).
- **Direct Inhibition:** antibiotics as **trimethoprim** compete with folate for absorption into intestinal cells.
- **Damaging mucosal cells** (**cancer chemotherapy** may damage mucosal cells).
- **Drug-Nutrient Binding**
 - 1- **bile acid binders** (which reduce cholesterol levels) bind to **fat-soluble** vitamins.
 - 2- Some **antibiotics**, notably **tetracycline** and **ciprofloxacin**, bind to the **calcium** in food.

3- Drugs Interacting Metabolism of Nutrients

A. Structural analogs:

1- **Methotrexate** similar **folate** in structure. Methotrexate, anti cancer, competes with folate for the enzyme that converts folate to its active form

2- **Isoniazid (INH)**, anti-tuberculosis, which is similar in structure to **vitamin B6** and can interfere with the vitamin's conversion to its active form, vitamin B6 supplements are often given.

B. Similar enzyme systems: sharing the same enzymes in the small intestine and liver

1- Anticonvulsants **phenobarbital** and **phenytoin** increase levels of the liver enzymes that metabolize **folate, vitamin D, and vitamin K**; so supplements of these vitamins are given.

C. Competing for transport on plasma proteins (fatty acids and drugs may compete for the same sites on the plasma protein albumin).

4- Drug Effects on Nutrient Excretion

- Some **diuretics** as **furosemide** that enhance urinary excretion resulting in greater urinary excretion of **calcium, potassium, magnesium, and thiamin**.

Note: dietary supplements may be necessary

- Causing diarrhea or vomiting (diarrhea and vomiting may cause electrolyte losses).
- The increased urinary losses of electrolytes caused by **aminoglycoside antibiotics**

- 1- Nutrients May Alter Drug Absorption**
- 2- Interactions with Dietary Components**
- 3- Dietary Effects on Drug Metabolism**
- 4- Dietary Effects on Drug Excretion**
- 5- Diet-Drug Interactions and Toxicity**

Effect of Nutrients on Drug

1- Nutrients May Alter Drug Absorption

Most drugs are absorbed in the upper small intestine. Major influences on drug absorption include **Stomach-Emptying Rate & Stomach Acidity** :

a- Stomach-Emptying Rate:

- Altering rate of gastric emptying (intestinal absorption of drugs **delayed** when taken **with food**).

Drugs to be Taken on an EMPTY Stomach

1. **Antihistamines: Claritin and Zyrtec.**
2. **Analgesics/Antipyretics: Ex. Acetaminophen**

Drugs to be Taken on an FULL Stomach

1- Analgesics/Anti-inflammatories: NSAIDS, Ibuprofen & Aspirin.



- **Aspirin** irritates the stomach and increases gastric bleeding; a buffered or enteric-coated form of Aspirin may be given.

2. Lovastatin

- This drug is **poorly absorbed without food**, so this drug should be taken with an **evening meal**



b- Stomach Acidity:

- Some drugs are better absorbed in an acidic environment and when conditions are alkaline (use of anti-acid drugs), reduce their absorption
- **Ketoconazole**, antifungal agent, is absorbed better with meals (due to increased acid secretion).

2- Interactions with Dietary Components

- Binding to drugs (**calcium** binds to **tetracycline**, reducing drug and calcium absorption)
- **High-fiber** diets may decrease the absorption of some **tricyclic antidepressants**
- Competing for absorption sites in the intestine (dietary **amino acids** interfere with **levodopa** absorption).

3- Dietary Effects on Drug Metabolism

1- Structural analogs:

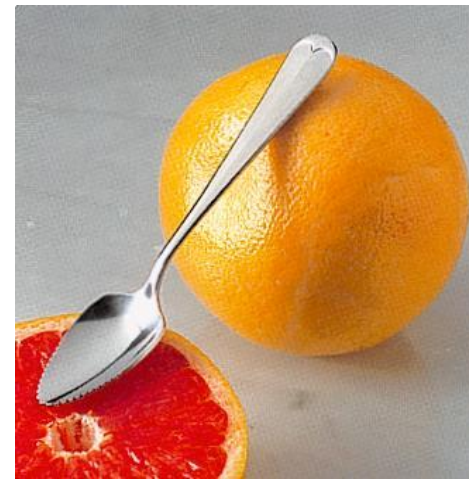
Warfarin, anticoagulant drug, and **vitamin K** are structurally similar, so warfarin blocks the enzyme that activates vitamin K, preventing the synthesis of blood-clotting factors. Some herbs may enhance the activity of warfarin and therefore should be avoided during warfarin treatment, such as **garlic, ginseng**.

2- Similar enzyme systems:

sharing the same enzymes in the small intestine and liver

Grapefruit:

Compounds in **grapefruit** have been found to **inhibit or inactivate** **cytochrome P450** that metabolize a number of different drugs. So blood concentrations of the drugs increase, leading to stronger physiological effects.



Drugs which may interact with Grapefruit Juice

- 1. Antihistamines.**
- 2. Benzodiazepines.**
- 3. Calcium Blockers.**
- 4. Cholesterol Lowering Drugs.**
- 5. Immune system suppressants.**

4- Dietary Effects on Drug Excretion

Some food components can alter drug reabsorption by the kidneys. For example, the amount of **lithium** drug reabsorbed by the kidneys is similar to the amount of **sodium** reabsorbed. so increase of sodium depletion or dehydration, where sodium reabsorption is increased, leading to lithium retention. Similarly, a person with a high sodium intake will excrete more sodium in the urine, and therefore more lithium.

Urine acidity affects drug excretion due to the effects of pH. E.g. **Quinidine**, used to treat arrhythmias, is excreted more readily in **acidic urine**. Foods cause urine to become more alkaline e.g. (**vegetables & fruits**) may reduce quinidine excretion and raise its blood levels.

5- Diet-Drug Interactions and Toxicity

1) The combination of **Tyramine** (a food component) and **monoamine oxidase (MAO) inhibitors**, antidepressants, **can be fatal**.

Tyramine, occurs naturally in foods and is also formed when bacteria degrade the protein in foods.

MAO inhibitors block an enzyme that normally inactivates **tyramine** as well as epinephrine and norepinephrine.

Patients who take MAO inhibitors consume excessive tyramine, the increased tyramine in the blood can induce a sudden release of accumulated norepinephrine resulting in severe headaches, rapid heartbeat, and a dangerous rise in blood pressure.

Patients who take MAO inhibitors should restrict their intakes of tyramine.

2) Increasing side effects of the drug (**caffeine** can **increase** adverse effects of drug).

3) **Increasing drug action** to excessive levels (**grapefruit** components may **block** metabolism of drugs and **enhance** drugs' actions and side effects).

4) **Alcohol:**

- Acts as gastric irritant; in combination with other irritants such as **NSAIDs** may increase chance of GIT bleed

- With **CNS-suppressant** drugs may produce excessive drowsiness, incoordination

- Should not be combined with other **hepatotoxic** drugs such as **acetaminophen, amiodarone, methotrexate**

HOW TO Prevent Diet-Drug Interactions???

- The appropriate method of administration (twice daily or at bedtime).
- How the medication should be administered with respect to foods, and specific nutrients (for example, take on an empty stomach, take with food, do not take with milk).
- How the medication should be used with respect to other medications.
- The side effects that may affect food intake (nausea and vomiting, constipation or diarrhea, or sedation, for example) or nutrient needs (interference with nutrient absorption or metabolism, for example).