

NUTRITIONAL BIOCHEMISTRY (Sem VI)

Pharmacological aspects of food-drug interactions

Pharmacodynamics is the study of the biochemical and physiological effects of a drug. This response may be enhanced or attenuated by the addition of other substances with similar or opposing actions.

Pharmacokinetics is the study of the time course of a drug in the body. It involves:

- Absorption: Movement of drug from the site of administration to the bloodstream.
- Distribution: This occurs when the drug leaves the systemic circulation and travels to various organs of the body.
- Metabolism: Transformation of a drug from a lipid soluble to a more water-soluble compound that can be handled easily by the kidneys.
- Excretion: Elimination of drugs and drug metabolites from the body.

Medication is administered to produce a pharmacologic affect in the body, or a specific organ or tissue. To achieve this goal, the drug must move from the site of administration into the bloodstream and then to the site of its action. An interaction between the drug and the food or a nutrient can alter this process at any point. Below are described the types of food-drug interactions.

A. Effect of food on drug therapy

Drug absorption			
	Drug	Type of drug	Interaction with food
1.	Ciprofloxacin Tetracycline	Antibiotics	Form insoluble compounds with calcium in dairy products or calcium fortified foods/beverages, magnesium, zinc, or aluminum in antacids, thus reducing the absorption of both the drug and the nutrient.
2.	Alendronate Risedronate	Anti-osteoporotic	Absorption is negligible if these drugs are taken with food and reduced by 60% if taken with coffee or orange juice.
3.	Encaptone	Anti-parkinsonian	Chelates with iron; hence iron must be taken 1h before or 2h after taking this drug.
4.	Lanoxin	Cardiovascular	Should not be taken with high phytate foods like wheat bran or oatmeal.
5.	Cefuroxime axetil/ saquinavar	Antibiotic/ antiretroviral	Absorption of these drugs is increased in the presence of food in the stomach. Hence, they are advised to be taken along with or immediately after a meal.
6.	Famotidine/ Omeprazole	Antacids/ Proton pump inhibitors	Drugs like these which alter the gastrointestinal pH can interfere with the absorption of antifungal drugs like ketoconazole. Ingestion of ketoconazole with cola (which decreases the pH of the gut) can increase its bioavailability.
Medication and Enteral Nutrition Interactions			
1.	Chlorpromazine	Antibiotic	Suspensions of this can cause granulation and gel formation and can clog feeding tubes and interrupt delivery of the nutrient.
Drug distribution			
1.	Warfarin	Anticoagulant	Warfarin is 99.9% bound to serum proteins. Low albumin

			levels (typically in older people) can cause more of free drug in the body, leading to excessive anticoagulation and bleeding. It also reduces the hepatic production of four vitamin K dependent clotting factors.
2.	Phenytoin	Anticonvulsant	Phenytoin is more than % bound to serum proteins. Low albumin levels (typically in older people) can cause more of free drug in the body, leading to phenytoin toxicity.
Drug metabolism			
1.	Theophylline	Anti-asthmatic	A diet rich in protein and low in carbohydrates can increase the metabolism of this drug in the liver.
2.	Simvastatin, atorvastatin / Felodipine	HMG-CoA reductase inhibitors/ calcium channel blocker	Grapefruit and Seville oranges inhibit the cytochrome P-450 3A4 enzyme system responsible for the oxidative metabolism of these drugs. This increase in blood levels of unmetabolized drug by the ingestion of these fruits results in a greater pharmacologic effect and possible toxicity. Statins also affect the formation of Coenzyme Q ₁₀ and hence at least 100mg CoQ ₁₀ daily is given to such patients.
Drug excretion			
1.	Lithium	Anti-manic	In conditions of low sodium or dehydration, kidneys absorb more sodium. However, if a person is treated with lithium, then alongside sodium, lithium is also resorbed, leading to possible toxicity. Like sodium, more of lithium is also eliminated from the kidneys, leading to a therapeutic failure.
2.	Memantine	Used to treat Alzheimer's	Urinary alkalinizers (foods which increase the urinary pH) like milk and vegetables can decrease the excretion of this drug, leading to its higher blood levels and increasing the risk of toxicity.

B. Effects of drugs on food and nutrition

Nutrient absorption			
1.	Ciprofloxacin Tetracycline	Antibiotics	Forms insoluble compounds with calcium in dairy products or calcium fortified foods/beverages, magnesium, zinc, or aluminum in multivitamin tablets, thus reducing the absorption of both the drug and the nutrient.
2.	Furosemide, sulfamethoxazole / misoprostol	Laxatives containing sorbitol/ gastric mucosa protectant	Reduces transit time of food and nutrients in the gut and may cause diarrhea, leading to loss of calcium and potassium.
3.	Famotidine/ Omeprazole	Antacids/ Proton pump inhibitors	Inhibits gastric acid secretion and raises gastric pH. This impairs absorption of vitamin B12 by reducing its cleavage from the dietary sources.
4.	Cimetidine	Histamine H ₂ receptor antagonist	Inhibits secretion of Intrinsic factor, and can cause vitamin B12 deficiency.
5.	Colchicine/	Anti-	These drugs damage the villi and the microvilli. They

	Paraaminosalicylic acid	inflammatory/ anti-TB (NSAID)	inhibit the brush border enzymes and the intestinal transport systems involved in nutrient absorption. This impairs absorption of vitamin B12. NSAIDs may also cause colitis, leading to diarrhea, weight loss and iron deficiency anemia.
6.	Sulfasalazine/ Trimethoprim	Against ulcerative colitis/ NSAID	These drugs damage the villi & the microvilli, and inhibit the brush border enzymes & the intestinal transport systems involved in nutrient absorption. These particular drugs are competitive inhibitors of folate transport mechanism.
Nutrient metabolism			
1.	Phenytoin, phenobarbital	Anticonvulsants	Induce hepatic enzymes and increase the metabolism of vitamin D, K and folic acid. Hence, supplements of these vitamins are prescribed with these drugs.
2.	Isoniazid/ Levodopa	Anti-TB/ Anti- Parkinsonian	Blocks conversion of pyridoxine to pyridoxal-5-phosphate. These drugs can cause pyridoxine deficiency in patients with low pyridoxine intake.
3.	Methotrexate	Folic acid antagonist	Leucovorin (folinic acid, the reduced form of folic acid) is given along with methotrexate to protect normal cells and prevent anemia & GI damage.
Nutrient excretion			
1.	Furosemide, bumetanide	Loop diuretics	Along with increasing the excretion of sodium, these drugs also increase the excretion of magnesium, calcium, sodium and chloride, and can cause hyponatremia.
2.	Hydrochlorothiazide	Thiazide diuretics	Increases the excretion of potassium and magnesium but reduces the excretion of calcium by enhancing its renal reabsorption.
3.	Enalapril, fosinopril	ACE inhibitors (anti- hypertensive)	These drugs decrease potassium excretion and increase serum potassium levels. A combination of potassium sparing diuretics (like spironolactone) and ACE inhibitors can increase the risk of hyperkalemia.
4.	Prednisone	Corticosteroids	Decreases sodium excretion and increase potassium and calcium excretion. Calcium and Vitamin D supplements are prescribed in case of long-term treatment with these corticosteroids.
5.	Chlorpromazine	Antipsychotic	Increases excretion of riboflavin and can cause riboflavin deficiency.
6.	Cisplatin		This causes increase in excretion of magnesium, leading to development of acute hypomagnesemia resulting from nephrotoxicity. Intravenous and oral supplementation of magnesium is recommended.

C. Modification of drug action by food and nutrients

	Combination of drug	Effect
1.	Monoamine oxidase (MAO) inhibitor phenelzine sulfate and pressor agent like dopamine or histamine	MAO inhibitors prevent the deamination of pressor agents and increase its life in the blood. However, too much of these pressor agents can cause increased heart rate, headache or even stroke.
2.	Caffeine with stimulant drugs like amphetamines and theophylline	Increases the stimulatory effects of these drugs.

3.	Warfarin with garlic, papaya, mango and ginseng (platelet inhibitor)	Enhances the anticoagulant effect of warfarin.
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D. Pyschoactive drugs

	Drug	Effect
1.	Lysergic acid diethylamide	Induces hallucination. Effects include altered thoughts, feelings and awareness of one's surroundings.
2.	Methamphetamine	It is a potent central nervous system stimulant.