Clinically relevant drug interactions in Dermatology

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Interactions affecting drug absorption

Dermatologic agent	Interaction	Mechanism	Effect	Comment
Azole antifungal agents	Antacids and H_2 blockers	Decreased absorption in presence of high pH	Decreased plasma azole antifungal agent	*Fluconazole absorption is not significantly influenced by gastric pH or food.*
Macrolide antibiotics	Digoxin	Increased GI absorption of digoxin by altering GI flora	Increased plasma digoxin	
Quinolones	Aluminum/magnesium containing antacids, calcium (milk and dairy products), zinc, iron	Decreased absorption due to formation of poorly absorbed complexes between quinolone and metal ions	Decreased plasma quinolone	*Administer one to two hours before, and not within four hours after, the ingested metal ions.*
Tetracyclines	Digoxin	Increased GI absorption of digoxin by altering GI flora	Increased plasma digoxin	
	Cholestyramine and colestipol	Decreased absorption	Decreased plasma tetracycline	
	Aluminum/magnesium containing antacids, calcium (milk and dairy products), zinc, iron	Decreased GI absorption due to the formation of poorly absorbed complexes between tetracycline and metal ions	Decreased plasma tetracycline	*Administer one to two hours before, and not within four hours after, the ingested metal ions. Doxycycline and minocycline may be administered with food or dairy products without causing a major reduction in absorption, but concurrent use of iron may reduce their absorption.*

Interactions affecting drug metabolism

Dermatologic agent	Interacting drug	Mechanism	Effect	Comment
Azathioprine	Allopurinol	Inhibition of the xanthine oxidase pathway and shifting to the HGPRT pathway	Excess formation of active metabolite leading to bone marrow suppression	*If used concomitantly, azathioprine dose should be reduced 1/3 to1/4. Monitoring of 6-thioguanine nucleotide is prudent.*
	ACE inhibitor	Unknown	Anemia or leukopenia	*Azathioprine-induced impairment of hematopoiesis and ACE inhibitor-induced decrease in erythropoietin may result in additive effects on bone marrow.*
Azole antifungal agents	Cyclosporine	Decreased metabolism	Increased plasma cyclosporine	
	Warfarin	Decreased metabolism	Increased plasma warfarin	
Bexarotene	Gemfibrozil	Decreased metabolism	Increased plasma concentrations of bexarotene with reports of massive hypertriglyceridemia and pancreatitis	*Thought to be at least partially related to CYP 3A4 inhibition by gemfibrozil. Atorvastatin and simvastatin are acceptable alternatives.*
Contraceptives, oral	Barbiturates, carbamazepine, phenytoin, rifampin, griseofulvin, St John's wort	Increased metabolism	Decreased plasma oral contraceptives	*Caused by induction of CYP 3A4.*
Fluconazole	CYP 2C9 substrates: phenytoin, sulfonylureas, NSAIDs, warfarin	Decreased metabolism	Increased plasma phenytoin, sulfonylureas, NSAIDs, warfarin	*Fluconazole is a strong inhibitor of CYP2C9.*

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Interactions affecting drug metabolism, cont'd

Dermatologic agent	Interacting drug	Mechanism	Effect	Comment
Gancyclovir	Zidovudine	Probably synergistic myelosuppression	Severe hematologic toxicity and pancytopenia	*The combination is poorly tolerated in patients with AIDS and serious-CMV disease, with 82% developing severe to life-threatening hematologic toxicity.*
Macrolide antibiotics	HMG-CoA reductase inhibitors	Decreased metabolism	Increased plasma HGM-CoA reductase inhibitor with myositis and rhabdomyolysis	*Does not occur with azithromycin. (Does not complex with hepatic oxidizing enzymes)*
	Quinolones	Probably pharmacodynamic (additive) effect	Life-threatening cardiac arrhythmias and risk of TdP	
	Warfarin	Decreased metabolism	Increased plasma warfarin	*Does not occur with azithromycin.*
Methotrexate	Trimethoprin, sulfonamides, and dapsone	Synergistic inhibition of the folic acid metabolic pathway	Increased hematologic toxicity	
	Phenytoin, phenothiazines, salicylates, tetracyclines, chloramphenicol, and sulfonamides	Increased methotrexate levels by displacement of plasma proteins	Increased toxicity	
	NSAIDs, salicylates, penicillins	Increased methotrexate levels due to decreased renal perfusion and methotrexate excretion	Increased toxicity	
Quinolones	Antiarrhythmic agents	Synergistic prolongation of the QT interval	Life-threatening cardiac arrhythmias, including TdP	
	Tricyclic antidepressants	Probably pharmacodynamic (additive) effect	Life-threatening cardiac arrhythmias and risk of TdP	
	Warfarin	Unknown	Increased anticoagulant effect of warfarin	
Retinoids, oral	Methotrexate	Probable pharmacodynamic (additive) effect	Increased risk of hepatitis	
	Tetracyclines	Additive or synergistic effect	Increased risk of pseudotumor cerebri	
Terbinafine	CYP 2D6 substrates: TCAs, SSRIs, antipsychotics, opioids, β-blockers, class I antiarrhythmics	Decreased metabolism	Increased plasma levels of TCA, SSRI, antipsychotic, opioid, β-blocker, class I antiarrhythmics	*Terbinafine is a strong inhibitor of CYP 2D6.*
Tetracyclines	Warfarin	Elimination of vitamin K-producing bacteria in the gut. Displacement of albumin-bound warfarin	Increased plasma warfarin	*Doxycycline is the most likely offender.*

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