PHARMACOLOGICAL EFFECTS OF COMMON MEDICATIONS WITH GRAPEFRUIT JUICE (Part 1 of 2)

Grapefruit is a healthy addition to a well-balanced diet. However, the fruit or juice has been shown to affect the metabolism of many medications, increasing the risk of toxicity and adverse events. Characteristics of oral medications that may interact with grapefruit include extensive metabolism through the intestinal cytochrome P450 3A4 (CYP3A4) system, low bioavailability, and a narrow therapeutic index. Grapefruit juice interacts through the intestinal CYP3A4 system and can inhibit the concentration for 24–72 hours.[1] This list is based on manufacturer's prescribing information and is not a complete list of medications that may interact with grapefruit. Caution should be taken by both patient and physician and monitor adverse reactions when taking medications that may interact with grapefruit or juice.

Brand	Generic	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
ALKALOID		
Colcrys	colchicine	Increases the risk of colchicine-induced toxic effects; significant increase in colchicine plasma concentration is anticipated. Grapefruit and grapefruit juice should not be consumed during colchicine treatment.
ANTIARRHYTHMICS		
Cordarone	amiodarone	Inhibits CYP3A4-mediated metabolism of oral amiodarone resulting in increase plasma levels of amiodarone. Avoid co-administration.
Multaq	dronedarone	Moderate inhibitor of CYP3A, results in a 3-fold increase in dronedarone exposure and a 2.5-fold increase in C_{max}. Avoid co-administration.
Tikosyn	dofetilide	Inhibitor of the CYP3A4 isoenzyme, thus could increase systemic dofetilide exposure. If co-administration is necessary, use with caution.
ANTIHELMINTHIC		
Biltricide	praziquantel	1.6-fold increase in the C_{max} and a 1.9-fold increase in the AUC of praziquantel.
ANTIPSYCHOTIC		
Orap	pimozide	Inhibits CYP3A4-mediated metabolism of pimozide. Avoid co-administration.
CALCIUM CHANNEL BLOCKERS		
Plendil	felodipine	2-fold increase in felodipine AUC and C_{max}. Avoid co-administration prior to and during treatment.
Procardia	nifedipine	2-fold increase in nifedipine AUC and C_{max} with no change in half-life. Avoid co-administration.
Sular	nisoldipine	3-fold increase in nisoldipine C_{max} and 2-fold increase in nisoldipine AUC. Avoid co-administration before and after dosing.
Verelan	verapamil	May significantly increase concentrations of verapamil. Increased S-and R-verapamil $AUC_{0\text{-}12}$ by 36% and 28%, respectively. Steady state C_{max} and C_{min} of S-verapamil increased by 57% and 16.7%, respectively compared to control. C_{max} and C_{min} of R-verapamil increased by 40% and 13%, respectively.
CHOLESTEROL-LOWERING MEDICATIONS		
Lipitor	atorvastatin	Inhibits CYP3A4 and can increase plasma concentrations of atorvastatin, especially with excessive grapefruit juice consumption (>1.2 liters per day).
Mevacor	lovastatin	Inhibits CYP3A4 and can increase plasma concentrations of lovastatin. Avoid large quantities of grapefruit juice (>1 quart daily).
Zocor	simvastatin	Inhibits CYP3A4 and can increase plasma concentrations of simvastatin and may increase risk of myopathy. Avoid large quantities of grapefruit juice (>1 quart daily).
CYSTIC FIBROSIS THERAPY		
Kalydeco	ivacaftor	Co-administration may increase exposure of ivacaftor. Grapefruit or Seville oranges should be avoided during treatment.
ERGOT ALKALOIDS		
D.H.E. 45	dihydroergotamine mesylate	A potential risk for serious toxicity (including vasospasm) exists.
	ergotamine tartrate + caffeine	A potential risk for serious toxicity (including vasospasm) exists.
H_1-RECEPTOR ANTAGONIST		
Allegra	fexofenadine	May reduce bioavailability and exposure of fexofenadine. In a bioequivalence study, the bioavailability of fexofenadine was reduced by 36%. Take with water.

(continued)

PHARMACOLOGICAL EFFECTS OF COMMON MEDICATIONS WITH GRAPEFRUIT JUICE (Part 2 of 2)

Brand	Generic	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
HYPONATREMIA THERAPY		
Samsca	tolvaptan	Co-administration results in a 1.8-fold increase in exposure to tolvaptan.
IMMUNOSUPPRESSANTS		
Neoral	cyclosporine	Affects metabolism and increases blood concentrations of cyclosporine. Avoid co-administration.
Prograf	tacrolimus	Affects CYP3A-mediated metabolism and should be avoided.
Rapamune	sirolimus	Reduces CYP3A4-mediated drug metabolism and must not be taken with or used for dilution of sirolimus.
Torisel	temsirolimus	May increase plasma concentrations of sirolimus, a major metabolite of temsirolimus, and should be avoided.
Zortress	everolimus	Inhibits CYP3A4 and P-gp activity and should therefore be avoided with concomitant use of everolimus and cyclosporine.
INTERMITTENT CLAUDICATION THERAPY		
Pletal	cilostazol	Increase in the C_{max} of cilostazol by ~ 50%, but has no effect on AUC.
MYELOFIBROSIS THERAPY		
Jakafi	ruxolitinib	The recommended starting dose of ruloxitinib is 10mg twice daily for patients with a platelet count $\geq 100 \times 10^9$/L. Concurrent administration of should be avoided in patients with platelet counts $<100 \times 10^9$/L.
ONCOLOGY AGENTS		
Afinitor	everolimus	May increase exposures of everolimus and should be avoided.
Inlyta	axitinib	May increase plasma concentrations of axitinib and should be avoided.
Ixempra	ixabepilone	May increase plasma concentrations of ixabepilone and should be avoided.
Sprycel	dasatinib	May increase plasma concentrations of dasatinib and should be avoided.
Sutent	sunitinib	May increase plasma concentrations of sunitinib and should be avoided.
Tasigna	nilotinib	May increase plasma concentrations of nilotinib and should be avoided.
Tykerb	lapatanib	May increase plasma concentrations of lapatinib and should be avoided.
Votrient	pazopanib	May increase plasma concentrations of pazopanib and should be avoided.
Xalkori	crizotinib	May increase plasma concentrations of crizotinib and should be avoided.
OPIOID		
Fentora	fentanyl	May result in a potentially dangerous increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression.
PHOSPHODIESTERASE TYPE 5 INHIBITORS		
Cialis	tadalafil	Likely increase of tadalafil exposure.
Staxyn	vardenafil	Do not use, as the systemic concentration of vardenafil is increased.
PSYCHOTROPIC AGENTS		
	buspirone	4.3 fold increase in C_{max}; 9.2 fold increase in AUC. Avoid drinking large amounts (200mL double-strength three times daily) of grapefruit juice.
Halcion	triazolam	Increases the C_{max} of triazolam by 25%, increases AUC by 48%, and increases half-life by 18%. Use with caution.
STEROID		
Entocort EC	budesonide	After extensive intake of grapefruit juice, the systemic exposure for oral budesonide increased about two times. Ingestion of grapefruit or grapefruit juice should be avoided.
NOTES		

[1]Stump AL, Mayo T, Blum A. Management of Grapefruit-Drug Interactions. *Am Fam Physician.* 2006 Aug 15;74(4):605-608.

AUC = area under the curve; C_{max} =max concentration

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