

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

Grapefruit or grapefruit 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 24–72hrs. Not an exclusive 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.

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
ALKALOID		
colchicine	Colcrys	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		
amiodarone	—	Inhibits CYP3A4-mediated metabolism of oral amiodarone resulting in increase plasma levels of amiodarone. Avoid co-administration.
dofetilide	Tikosyn	Inhibitor of the CYP3A4 isoenzyme, thus could increase systemic dofetilide exposure. If co-administration is necessary, use with caution.
dronedarone	Multaq	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.
ANTHELMINTHIC		
praziquantel	Biltricide	1.6-fold increase in the C_{max} and a 1.9-fold increase in the AUC of praziquantel.
ANTI PSYCHOTIC		
pimozide	Orap	Inhibits CYP3A4-mediated metabolism of pimozide. Avoid co-administration.
CALCIUM CHANNEL BLOCKERS		
felodipine	—	2-fold increase in felodipine AUC and C_{max} . Avoid co-administration prior to and during treatment.
nifedipine	Procardia	2-fold increase in nifedipine AUC and C_{max} with no change in half-life. Avoid co-administration.
nisoldipine	Sular	3-fold increase in nisoldipine C_{max} and 2-fold increase in nisoldipine AUC. Avoid co-administration.
verapamil	Verelan	May significantly increase concentrations of verapamil. Increased S- and R-verapamil AUC_{0-12} 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. No clinical consequences expected.
CHOLESTEROL-LOWERING MEDICATIONS		
atorvastatin	Lipitor	Inhibits CYP3A4 and can increase plasma concentrations of atorvastatin, especially with excessive grapefruit juice consumption (>1.2L/day).
lovastatin	—	Inhibits CYP3A4 and can increase plasma concentrations of lovastatin. Avoid co-administration.
simvastatin	Zocor	Inhibits CYP3A4 and can increase plasma concentrations of simvastatin and may increase risk of myopathy. Avoid co-administration.
CYSTIC FIBROSIS THERAPY		
ivacaftor	Kalydeco	Co-administration may increase exposure of ivacaftor. Grapefruit or Seville oranges should be avoided during treatment.
ERGOT ALKALOIDS		
dihydroergotamine mesylate	D.H.E. 45	A potential risk for serious toxicity (including vasospasm) exists.
ergotamine tartrate + caffeine	—	A potential risk for serious toxicity (including vasospasm) exists.
H₁-RECEPTOR ANTAGONIST		
fexofenadine	Allegra	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 GRAPEFRUIT JUICE WITH MEDICATIONS (Part 2 of 2)

Generic	Brand	Clinical Implications of Co-administration with Grapefruit or Grapefruit Juice
HYPONATREMIA THERAPY		
tolvaptan	Samsca	Co-administration results in a 1.8-fold increase in exposure to tolvaptan.
IMMUNOSUPPRESSANTS		
cyclosporine	Neoral	Affects metabolism and increases blood concentrations of cyclosporine. Avoid co-administration.
everolimus	Zortress	Inhibits CYP3A4 and P-gp activity and should therefore be avoided with concomitant use of everolimus and cyclosporine.
sirolimus	Rapamune	Reduces CYP3A4-mediated drug metabolism and must not be taken with or used for dilution of sirolimus.
tacrolimus	Prograf	Affects CYP3A-mediated metabolism and should be avoided.
temsirolimus	Torisel	May increase plasma concentrations of sirolimus, a major metabolite of temsirolimus, and should be avoided.
INTERMITTENT CLAUDICATION THERAPY		
cilostazol	—	Increase in the C_{max} of cilostazol by ~ 50%, but has no effect on AUC. Reduce dose to 50mg with co-administration.
MYELOFIBROSIS THERAPY		
ruxolitinib	Jakafi	The recommended starting dose of ruxolitinib 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		
axitinib	Inlyta	May increase plasma concentrations of axitinib and should be avoided.
crizotinib	Xalkori	May increase plasma concentrations of crizotinib and should be avoided.
dasatinib	Sprycel	May increase plasma concentrations of dasatinib and should be avoided.
everolimus	Afinitor	May increase exposures of everolimus and should be avoided.
ixabepilone	Ixempra	May increase plasma concentrations of ixabepilone and should be avoided.
lapatinib	Tykerb	May increase plasma concentrations of lapatinib and should be avoided.
nilotinib	Tasigna	May increase plasma concentrations of nilotinib and should be avoided.
pazopanib	Votrient	May increase plasma concentrations of pazopanib and should be avoided.
sunitinib	Sutent	May increase plasma concentrations of sunitinib and should be avoided.
OPIOID		
fentanyl	Fentora	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		
tadalafil	Cialis	Likely increase of tadalafil exposure.
vardenafil	Staxyn	Do not use, as the systemic concentration of vardenafil is increased.
PSYCHOTROPIC AGENTS		
bupirone	—	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.
triazolam	Halcion	Increases the C_{max} of triazolam by 25%, increases AUC by 48%, and increases half-life by 18%. Use with caution.
STEROID		
budesonide	Entocort EC	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.

REFERENCES

Stump AL, Mayo T, Blum A. Management of Grapefruit-Drug Interactions. *Am Fam Physician*. 2006 Aug 15;74(4):605-608. (Rev. 6/2018)