

A REVIEW ON THE DRUG-DRUG INTERACTIONS WITH METABOLISM AND BRAND NAMES" WITH SOME USES

MYLE AKSHAY KIRAN

DOCTOR OF PHARMACY PRATISTA INSTUTE OF PHARMACEUTICAL SCIENCE DURJPALLY CHEVMALA MANDALAM SURYAPETA TELANGAN.
Email: myle Akshay Kiran @gmail.com

Received: 25 December 2016, Revised and Accepted: 28 August 2017

ABSTRACT

Drug interactions are the harmful or beneficial effects of co administered medicinal products, these interaction may be synergistic or antogon istic pharmco kinetics or pharmaco dynamics, drug interactions exists between drugs anddrugs, drug and foods, drugs and herbs, benefits effects include convenience . Reduced toxicity and reduction.

Antihistimine, antihistimine, asthma, analgesic, typhoid, hypertension, tuberculosis antibiotics, filaria, rheumatoid arthritis, antipyritic, anticancer immunological diseases, ectopic pregnancy, fever, osteoarthritis and antipyritic, analgesic, hiv aids, chicken pox,Salicylate, phenytoin, estrogens, hmg coa reductase inhibitors, barbiturates, chloramphenical, antacids, anticoagulant.

When two or more drugs are administered concurrently or within a reasonable time or after each other (both prescription drugs and non prescription drugs are involved) , the result may be in difference, synergisim, potentation, antagonisim this is called AS .DRUG-DRUG INTRACTION. Drug metabolism interactions results in the increase of biological half life or reduction of clearance there requiring lower doses, imipramine reduces the clearance of epinephrine, some examples of the drugs that inhibit metabolism like Erythromycin, ketocanazole, fluxetin, cimitidine, Allopurinol , carbamazepine, phenobarbital, Rifampacin , and phenytoin. Risk of Therapeutic failure, stoppage of induced may lead to toxic concentration of substrate and induction may lead to formation of toxic metabolites.

Keyword: Drug Formulation and contain.

INTRODUCTION

Drug interactions are the harmful or beneficial effects of co administered medicinal products, these interaction may be synergistic or antogon istic pharmco kinetics or pharmaco dynamics, drug interactions exists between drugs anddrugs, drug and foods, drugs and herbs, benefits effects include convenience Reduced toxicity and reduction.

DEFINATION

When two or more drugs are administered concurrently or within a reasonable time or after each other (both prescription drugs and non prescription drugs are involved) , the result may be in difference, synergisim, potentation, antagonisim this is called AS .DRUG-DRUG INTRACTION

DRUG DRUG INTERACTIONS

ASTHMA

Salbutamol +(diuretic) furosmide-hypokalemiea(muscle weakness, paralysis) Salbutamol(sympathomimetic) +(beta blocker) propranolol-narrowing the air way vessels difficult in breathing severe inaccute attacks . Salbutamol brand names-aerotaz, salbrel

ANALAGESIC

Aspirin (ANALAGESIC) +(beta blocker) atenolol - effectiveness decreases and metabolism of atenolol increases
Brand name of atenolol - tenerific, atezon

ANTI HISTIMINE

CitriZen HCl (ANTI HISTIMINE) +theophylline (asthma) - decreases the clearance activity
Brand name of citriZen - allorox syrup, allatral tablet, antrin tablet.

TYPHOID

Norflaxacin +warfarin(anticoagulant) - enhances the effect of anticoagulant
Norflaxacin +NSAIDS (analgesic) - increase the risk of cns stimulant
Brand name of Norflaxacin - alfloX, bifloX norfloX

ANTI HYPERTENSION

Nifedipine +beta blocker - increase the chf, severe heart failure
Nifedipine +cimitidine - decreases the Nifedipine action through enzyme inhibition
Brand name of Nifedipine-adolat, procardia xl, nifedipine xl

ANTI TUBERCULOSIS

Rifampacin +cyclosporin - reduced the cyclosporin risk of organ rejection
Rifampacin +isoniazid - risk of liver damage
Rifampacin +pyrazinmide - risk of liver damage
Rifampacin +quinine - decreases the blood levels
Rifampacin brand name - acox, coxid, fampacin, rificillin,

ANTI BIOTICS

Ampicillin+tetracycline-decreases the effect
Ampicillin +atenolol - decreases the effect of ampicillin
Ampicillin +typhoid vaccine - decreases the immunological resp of typhoid vaccine

FILARIA

Alabindazole +clozapine - decreases the blood count Brand name of Alabindazole - albenzole, eskazole zentel, andizole

RHEUMATOID ARTHRITIS ANTICANCER, AUTOIMMUNODISORDERS, ECTOPIC PREGNANCY

Methotrexate sodium +penicillin - increase the risk of toxicity

Methotrexate +aminoglycosides - inhibit the GI absorption, decreases the GI absorption of Methotrexate sodium

FEVER , OSTEOARTHRITIS, ANALGESIC, ANTIPYRITIC

Nimesulide+furosimide - rate of binding action is decreased.

Nimesulide +tolubutimide, fibrates, salicylates - displacement of protein binding capacity

Nimesulide +sulphonylureas-increase the action of hypoglycemic agent

Brand name of nimesulide - nimulid, nisc, insulide gel

HIV AIDS, CHICKEN POX

Acicclair +ketocanazole - synergistic effect

Acicclair +probenid-half life time increases renal clearance

Acicclair +zidovidine - neurotoxic effects

OTHER INTRACTION AND ASSOCIATED WITH DISEASES

Salicylates

Interference with renal excretion of drugs that undergo active tubular secretion, salicylates renal excretion dependent on urinary pH when large doses used.

Clinically documented INTRACTION

Carbonic anhydrase inhibitors - increased acetazolamide serum concentration, increase salicylate toxicity due to decrease the pH

Corticosteroids-increased the salicylate elimination toxic effect on gastric mucosa

Phenytoin

Induces the hepatic microsomal drug metabolism

Corticosteroids - decreases the serum corticosteroids levels

Doxycycline - decreases the serum Doxycycline levels

Quinidine - decreases the serum Quinidine levels

Chloramphenicol - increased the serum phenytoin

ESTROGENS

Metabolism inducible, enter hepatic circulation of estrogen may be interrupted by alteration in bowel flora.

Ampicillin - interruption of enter hepatic circulation of estrogen.

Phenytoin - increased the estrogen metabolism

Rifampin - increased the estrogen metabolism

HMG COA REDUCTASE INHIBITORS

Lovostatin, simvastatin and to lesser extent, increase the risk of myopathy

Atazanavir - decreases the statin metabolism

Clofibrate-increased the risk of myopathy

Cyclosporin - decreased statin metabolism

Rifampin - increased the statin metabolism

Ritinovir - decreases the statin metabolism

CHLORAMPHENICAL

Inhibit hepatic drug metabolizing enzyme

Phenytoin - decreases phenytoin metabolism

Sulfonylureas - decreases the Sulfonylureas metabolism

Calcium channel blockers

Cyclosporin - decreased cyclosporin metabolism

Rifampin - increased the metabolism of calcium channel blocker

BARBITURATES

Tacrolimus - increased the Tacrolimus metabolism

Theophylline - increased the theophylline metabolism reduced theophylline effect

ANTIFUNGAL azole derivative

Barbiturate - increased metabolism of itraconazole

Anticoagulant

NSAIDS - inhibit the platelet function

Simvastatin - decreases the warfarin metabolism

Barbiturate - enzyme induction

ANTACIDS

antacids may absorb drugs in gastrointestinal tract, reducing absorption, antacid tend to speed gastric emptying

Atazanavir - decreases the absorption of Atazanavir

Itraconazole - reduced gastrointestinal absorption of itraconazole due to increase pH

Tetracycline - decreases gastrointestinal absorption of Tetracycline

Allopurinol - inhibit the hepatic drug metabolism enzyme

+anticoagulant - increased the hypo pro thrombinemia effect

MONITORING AND MANAGING DRUG INTERACTIONS

IT is important to understand the patient current medication, including drugs prescribed by other physician, herbal products and nutrition supplements, dialogue with patients about diet and alcohol consumption is required, the goals of the medication therapy should be fewest drugs in the lowest doses for the short test possible period, the Pharmacology effect expected, wanted and unwanted, of all drugs taken should be determined because these effects usually include the spectrum of drug interaction as far as possible, drugs with wide margin should be preferable so that unexpected interaction do not lead to toxicity effects,

Monitoring Patients

Monitoring of patients after a change of treatments is important as some interaction may take about week of more time to observe, if dosage adjustments does not work, the drug may be replaced with another one which has lesser interaction, there are many sources available as reference tools for verification of the drug interaction, some of the sources are metck manual, drugs. Com, rxlist. Com,, drug has specific tool I. E INTRACTION checker for verifying drug interactions, with this tool persons can verify the interaction of many drug, informed decisions saves lives,

DISCUSSION

Drug interactions are the harmful or beneficial effects of co administered medicinal products, these interaction may be synergistic or antagonistic pharmacokinetics or pharmacodynamics, drug interactions exists between drugs and drugs, drug and foods, drugs and herbs, benefits effects include convenience

Reduced toxicity and reduction,, Synergistic interaction are those that give added benefits

Examples of synergistic drug interaction increase the analgesic effect of paracetamol with codeine, reduction of bacterial resistance with co administration of clavonic acid with Amoxicillin cytotoxic drugs combination in treatment of cancer requires lower doses, of each drug to obtain better Therapeutic effects with less side effects, saquinaver is poorly absorbed, treatment is three times dosing when combined with Ritinovir there is multiple features increasing the blood concentration , antagonism interaction are those may interact and coneract the action of one another example is oxybutin in for treating incontinence in a patients taking donepezil for alzheimers diseases and also alcohol and caffeine , phenobarbital and cimitidine, acetylcholine and ATROPINE,.

Results of drug drug interactions

Pharmacodynamic interaction are the actions that you are produced by the drug on the body, one drug alter the sensitive, or responsiveness of the body to other drug by producing antagonism, effect, pharmacokinetics interactions are the action that are produced by the body on drugs, these interaction affect the intensity and duration of the drug action and not the effect, they usually alter drug absorption, distribution, metabolism, and excretion on of another drug nisim this is called AS .DRUG-DRUG INTRACTION. Drug metabolism interactions results in the increase of biological half life or reduction of clearance there requiring lower doses, imipramine reduces the clearance of epinephrine, some examples of the drugs that inhibit metabolism like Erythromycin, ketocanazole, flutetin, cimitidine, Allopurinol , carbamazepine, phenobarbital, Rifampin , and phenytoin. Risk of Therapeutic failure, stoppage of induced may

lead to toxic concentration of substrate and induction may lead to formation of toxic metabolites.

CONCLUSION

TETRACYCLINE AND QUINOLINES form insoluble complexes with metals and there by their absorption is reduced that I'd reason for advising to avoid antacids preparations, milk products with certain products, some drugs reduced, absorbed and causes effects, absorption of Methotrexate or digixin by cholestyramine, antacids also alters pH decreases the absorption of weak acids and increasing the absorption of the weak bases, prealtic movements regulates the passage of drugs, laxatives causes the drug to move rapidly through the intestine resulting poor drug absorption

REFERENCES

MERCK.MANNUAL
DRUGS.COM
RXLIST.COM
DRUGS DESCRIPTION.COM
TRIPATI PHARMACOLOGY
ROGER WALKER THERPEUTICS
antibiotics and infection. Com
medicinalchemistry.com
community pharmacy. Com
hospital pharmacy. Com

REFERENCES

1. Ancrenaz V, Daali Y, Fontana P et al. Impact of polymorphisms and drugdrug interactions on clopidogrel and prasugrel response variability. *Curr Drug Metabo.* 2010; 11:667-77.
2. Nguyen TA, Dioda JG, Pharand C. Resistance to clopidogrel: a review of the evidence. *J Am Coll Cardiol.* 2005; 45(8):1157-64.
3. Wang Y, Wang Y, Zhao X et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med.* 2013; 369:11-19.
4. Steinhubl SR, Berger PB, Mann JT et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. *J Am Med Assoc.* 2002; 288(19):2411-20.
5. Yusuf S, Zhao F, Mehta SR et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001; 345(7):494-502.
6. Leon MB, Baim DS, Popma JJ et al. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. *N Engl J Med.* 1998; 339(23):1665-71.
7. Bha DL, Scheiman J, Abraham NS et al. ACCF/ACG/AHA Expert consensus document on reducing the gastrointestinal risk of antiplatelet therapy and NSAID use. *J Am Coll Cardiol.* 2008; 52(18):1502-17.
8. Gilard M, Arnaud B, Cornily JC et al. Influence of omeprazole on the antiplatelet action of clopidogrel associated with aspirin. *J Am Coll Cardiol.* 2008; 51(3):256-60.
9. Juurlink DN, Gomes T, Ko DT et al. A population-based study of the drug interaction between proton pump inhibitors and clopidogrel. *Can Med Assoc J.* 2009; 180(7):713-8.
10. Ho PM, Maddox TM, Wang L et al. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. *J Am Med Assoc.* 2009; 301(9):937-44.
11. Sibbing D, Morath T, Stegherr J et al. Impact of proton pump inhibitor on the antiplatelet effects of clopidogrel. *Throm Haemost.* 2009; 101(4):714-9.
12. Siller-Matula JM, Spiel AO, Lang IM et al. Effects of pantoprazole and esomeprazole on platelet inhibition by clopidogrel. *Am Heart J.* 2009; 157(1):148e1-e5.
13. Dunn SP, Steinhubl SR, Bauer D et al. Impact of proton pump inhibitor therapy on the efficacy of clopidogrel in the CAPRIE and CREDO trials. *J Am Heart Assoc.* 2013; 2(1):e004564
14. Kowk CS, Loke YK. Meta-analysis: the effects of proton pump inhibitors on cardiovascular events and mortality in patients receiving clopidogrel. *Aliment Pharmacol Ther.* 2000; 14:1191-98
15. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106(25):3143-421.
16. Kamanna VS, Ganji SH, Kashyap ML. Recent advances in niacin and lipid metabolism. *Curr Opin Lipidol.* 2013;24(3):239-45.
17. Digby JE, Ruparelia N, Choudhury RP. Niacin in cardiovascular disease: recent preclinical and clinical developments. *Arterioscler Thromb Vasc Biol.* 2012;32(3):582-8.
18. Villines TC, Kim AS, Gore RS et al. Niacin: the evidence, clinical use, and future directions. *Curr Atheroscler Rep.* 2012;14(1):49-59.
19. HPS2-THRIVE Collaborative Group. HPS2-THRIVE randomized placebo-controlled trial in 25 673 high-risk patients of ER niacin/laropiprant: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. *Eur Heart J.* 2013;34(17):1279-91.
20. Stone NJ, Robinson J, Lichtenstein AH et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013[epub ahead of print].
21. Pieper JA. Overview of niacin formulations: differences in pharmacokinetics, efficacy, and safety. *Am J Health Syst Pharm.* 2003;60(13 Suppl 2):S9-14;quiz S25.
22. Bhardwaj SS, Chalasani N. Lipid-lowering agents that cause drug-induced hepatotoxicity. *Clin Liver Dis.* 2007;11(3):597-613, vii.
23. McKenney J. Niacin for dyslipidemia: considerations in product selection. *Am J Health Syst Pharm.* 2003;60(10):995-1005.
24. Kelley VE, Fere A, Izui S et al. A fish oil diet rich in eicosapentaenoic acid reduces cyclooxygenase metabolites, and suppresses lupus in mrl-lpr mice. *J Immunol.* 1985; 134(3):1914-19.
25. Kar S, Webel R. Fish oil supplementation and coronary artery disease: does it help? *Mo Med.* 2012; 109(2):141-5.
26. Weitz D, Weintraub H, Fisher E et al. Fish oil for the treatment of cardiovascular disease. *Cardiol Rev.* 2010; 18(5):258-69.
27. Shahar E, Folsom AR, Dennis BH et al. Association of intake and dietary n-3 polyunsaturated fatty acids with a hypocoagulable profile. The atherosclerosis risk in communities (ARIC) study. *Arterioscler Thromb Vasc Biol.* 1993; 13: 1205-12.
28. Kim DN, Eastman A, Baker JE et al. Fish oils, atherogenesis, and thrombogenesis. *Ann NY Acad Sci.* 1995; 748:474-80.
29. Kaminski WE, Jendraschak E, Kier E et al. Dietary omega-3 fatty acids lower levels of platelet-derived growth factor mRNA in human mononuclear cells. *Blood.* 1993; 81:1871-9.
30. Mayer K, Merfelds M, Muhly-Reinholz M et al. Omega-3 fatty acids suppress monocyte adhesion to human endothelial cells: role of endothelial PAF generation. *Am J Physiol Heart Circ Physiol.* 2002; 283:H811-8.
31. Buckley MS, Go AD, Knapp WE. Fish oil interaction with warfarin. *Ann Pharmacother.* 2004; 38:50-3.
32. Eritsland J, Arnesen H, Seljeot I et al. Long-term effects of n-3 polyunsaturated fatty acids on haemostatic variables and bleeding episodes in patients with coronary artery disease. *Blood Coagul Fibrinolysis.* 1995; 6:17-22
33. Bender NK, Kraynak MA, Chique E et al. Effects of marine fish oils on the anticoagulation status of patients receiving chronic warfarin therapy. *J Thromb Thrombolysis.* 1998; 5:257-61.

34. Bays HE. Safety considerations with omega-3 fatty acid therapy. *Am J Cardiol.* 2007; 99:35C-43C.
35. Fung WT, Subramaniam G, Lee J et al. Assessment of extracts from red yeast rice for herb-drug interaction by in-vitro and in-vivo assays. *Sci Rep.* 2012;2:298.
36. Gordon RY, Becker DJ. The role of red yeast rice for the physician. *Curr Atheroscler Rep.* 2011;13(1):73-80.
37. Childress L, Gay A, Zargar A et al. Review of red yeast rice content and current Food and Drug Administration oversight. *J Clin Lipidol.* 2013;7(2):117-22
38. Klimek M, Wang S, Ogunkanmi A. Safety and efficacy of red yeast rice (*Monascus purpureus*) as an alternative therapy for hyperlipidemia. *P T.* 2009;34(6):313-27.
39. Chen CH, Uang YS et al. Interaction between Red Yeast Rice and CYP450 Enzymes/P-Glycoprotein and Its Implication for the clinical pharmacokinetics of lovastatin. *Evid Based Complement Alternat Med.* 2012;2012:127043.
40. European Association for Cardiovascular Prevention & Rehabilitation, Rainer Z, Catapano AL, De Backer G et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J.* 2011;32(14):1769-818.
41. Heber D, Lembertas A, Lu QY et al. An analysis of nine proprietary Chinese red yeast rice dietary supplements: implications of variability in chemical profile and contents. *J Altern Complement Med.* 2001;7(2):133-9.
42. Gordon RY, Cooperman T, Obermeyer W et al. Marked variability of monacolin levels in commercial red yeast rice products: buyer beware! *Arch Intern Med.* 2010;170(19):1722-7.
43. Ernst E. The risk-benefit profile of commonly used herbal therapies: Ginkgo, St. John's Wort, Ginseng, Echinacea, Saw Palmetto, and Kava. *Ann Intern Med.* 2002;136(1):42-53. Review.
44. Linde K, Berner MM, Kriston L. St John's wort for major depression. *Cochrane Database Syst Rev.* 2008; (4):CD000448. Review.
45. Shelton RC, Keller MB, Gelenberg A et al. Efficacy of St John's wort in major depression: a randomized controlled trial. *JAMA.* 2001;285(15):1978-86.
46. 46. Hypericum Depression Trial Study Group. Effect of *Hypericum perforatum* (St John's wort) in major depressive disorder: a randomized controlled trial. *JAMA.* 2002;287(14):1807-14.
47. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder, Third Edition. <http://psychiatryonline.org/content.aspx?bookid=28§ionid=1667485#654006>. (accessed 2014 Jan 20).
48. Benne D A Jr, Phun L, Polk JF et al. Neuropharmacology of St. John's Wort (*Hypericum*). *Ann Pharmacother.* 1998;32(11):1201-8. Review.
49. Müller WE, Singer A, Wonnemann M, et al. Hyperforin represents the neurotransmitter reuptake inhibiting constituent of hypericum extract. *Pharmacopsychiatry.* 1998;31 Suppl 1:16-21.
49. Markowitz JS, Donovan JL, DeVane CL et al. Effect of St John's wort on drug metabolism by induction of cytochrome P450 3A4 enzyme. *JAMA.* 2003;290(11):1500-4.
50. IMS Institute for Healthcare Informatics. The Use of Medicines in the United States: Review of 2010. http://www.imshealth.com/imshealth/Global/Content/IMS%20Institute/Documents/IHII_UseOfMed_report%20.pdf. (accessed 2013 Jan 20).
51. Dürr D, Seger B, Kullak-Ublick GA et al. St John's wort induces intestinal P-glycoprotein/MDR1 and intestinal and hepatic CYP3A4. *Clin Pharmacol Ther.* 2000; 68:598-604.
52. Andrés L, Andreasson A, Eggertsen R. Interaction between a commercially available St. John's wort product (Movina) and atorvastatin in patients with hypercholesterolemia. *Eur J Clin Pharmacol.* 2007;63(10):913-6.
53. Kullak-Ublick GA, Becker MB. Regulation of drug and bile salt transporters in liver and intestine. *Drug Metab Rev.* 2003;35(4):305-17. Review.
54. Moore LB, Goodwin B, Jones SA et al. St. John's wort induces hepatic drug metabolism through activation of the pregnane X receptor. *Proc Natl Acad Sci U S A.* 2000;97:7500-7502.
55. Dahan A, Altman H. Food-drug interaction: grape fruit juice augments drug bioavailability--mechanism, extent and relevance. *Eur J Clin Nutr.* 2004;58(1):1-9. Review.
56. Zhou S, Chan E, Pan SQ et al. Pharmacokinetics in interactions of drugs with St John's wort. *J Psychopharmacol.* 2004;18(2):262-76.
57. Sugimoto K, Ohmori M, Tsuruoka S et al. Different effects of St John's wort and the pharmacokinetics of simvastatin and pravastatin. *Clin Pharmacol Ther.* 2001;70(6):518-24.
58. Eggertsen R, Andreasson A, Andrés L. Effects of treatment with a commercially available St John's Wort product (Movina) on cholesterol levels in patients with hypercholesterolemia treated with simvastatin. *Scand J Prim Health Care.* 2007;25(3):154-9.
59. Iuliano L, Mauriello A, Sbarigia E et al. Radiolabeled low-density lipoprotein injected into patients with carotid stenosis accumulates in macrophages of atherosclerotic plaque: effect of vitamin E supplementation. *Circulation.* 2000;101(11):1249-54.
60. Tsimikas S, Brilakis ES, Miller ER et al. Oxidized phospholipids, Lp(a) lipoprotein, and coronary artery disease. *N Engl J Med.* 2005;353(1):4657.
61. Centers for Disease Control and Prevention. Health, United States, 2012. Selected prescription drug classes used in the past 30 days, by sex and age: United States, selected years 1988-1994 through 2007-2010. <http://www.cdc.gov/nchs/data/health/health12.pdf#092>. (accessed 2013 January 20th).
62. Lilja JJ, Neuvonen M, Neuvonen PJ. Effects of regular consumption of grapefruit juice on the pharmacokinetics of simvastatin. *Br J Clin Pharmacol.* 2004;58(1):56-60.
63. Fuhr U. Drug interactions with grape fruit juice. Extent, probable mechanism and clinical relevance. *Drug Saf.* 1998;18(4):251-72. Review.
65. Kantola T, Kivistö KT, Neuvonen PJ. Grapefruit juice greatly increases serum concentrations of lovastatin and lovastatin acid. *Clin Pharmacol Ther.* 1998;63(4):397-402.
64. Lilja JJ, Kivistö KT, Neuvonen PJ. Grapefruit juice-simvastatin interaction: effect on serum concentrations of simvastatin, simvastatin acid, and HMG-CoA reductase inhibitors. *Clin Pharmacol Ther.* 1998;64(5):477-83.
65. Lilja JJ, Kivistö KT, Neuvonen PJ. Grapefruit juice increases serum concentrations of atorvastatin and has no effect on pravastatin. *Clin Pharmacol Ther.* 1999;66(2):118-27.
66. Lilja JJ, Neuvonen M, Neuvonen PJ. Effects of regular consumption of grapefruit juice on the pharmacokinetics of simvastatin. *Br J Clin Pharmacol.* 2004;58(1):56-60.
67. Fukazawa I, Uchida N, Uchida E et al. Effects of grapefruit juice on pharmacokinetics of atorvastatin and pravastatin in Japanese. *Br J Clin Pharmacol.* 2004;57(4):448-55.
68. Ando H, Tsuruoka S, Yanagihara H et al. Effects of grapefruit juice on the pharmacokinetics of pitavastatin and atorvastatin. *Br J Clin Pharmacol.* 2005;60(5):494-7.
69. Go AM Jr. Safety and standard therapy: reconsidering the risks and benefits. *Arch Intern Med.* 2003;163(6):657-9.
70. Phillips PS, Haas RH, Bannykh S et al. Statin-associated myopathy with normal creatine kinase levels. *Ann Intern Med.* 2002;137(7):581-5.
73. Corsini A, Bellosta S, Bae R et al. New insights into the pharmacodynamic and pharmacokinetic properties of statins. *Pharmacol Ther.* 1999;84(3):413-28. Review.
71. Kajinami K, Takekoshi N, Brousseau ME et al. Pharmacogenetics of HMG-CoA reductase inhibitors: exploring the potential for genotype-based individualization of coronary heart disease management. *Atherosclerosis.* 2004;177(2):219-34.
72. Omar MA, Wilson JP. FDA adverse event reports on statin-associated rhabdomyolysis. *Ann Pharmacother.*

2002;36(2):288-95. Review. 76. Mazokopakis EE. Unusual causes of rhabdomyolysis. Intern Med J.