

- 17) Silverman RB.: Mechanism-based enzyme inactivation: Chemistry and Enzymology. vol 1. Boca Raton (FL): CRC Press, (1988): 224
- 18) Chan WK, Nguyen LT, Miller VP, Harris RZ: Mechanism-based inactivation of human cytochrome P450 3A4 by grapefruit juice and red wine. *Life Sci* (1998) 62:PL135-42
- 19) Bailey DG, Dresser GK, Kreeft JH, Munoz C, Freeman DJ, Bend JR.: Grapefruit-felodipine interaction: effect of unprocessed fruit and probable active ingredients. *Clin Pharmacol Ther.* 2000 (2000) Nov;68:468-77
- 20) Tassaneeyakul W, Guo LQ, Fukuda K, Ohta T, Yamazoe Y: Inhibition selectivity of grapefruit juice components on human cytochromes P450. *Arch Biochem Biophys* (2000) 378:356-63
- 21) Schmiedlin Ren P, Edwards DJ, Fitzsimmons ME, He K, Lown KS, Woster PM, Rahman A, Thummel KE, Fisher JM, Hollenberg PF, Watkins PB: Mechanisms of enhanced oral availability of CYP3A4 substrates by grapefruit constituents. Decreased enterocyte CYP3A4 concentration and mechanism-based inactivation by furanocoumarins. *Drug Metab Dispos* (1997) 25:1228-33
- 22) Bailey DG, Dresser GK, Bend JR: Bergamottin, lime juice, and red wine as inhibitors of cytochrome P450 3A4 activity: comparison with grapefruit juice. *Clin Pharmacol Ther* (2003) 73:529-37
- 23) Lown KS, Mayo RR, Leichtman AB, Hsiao HL, Turgeon DK, Schmiedlin Ren P, Brown MB, Guo W, Rossi SJ, Benet LZ, Watkins PB: Role of intestinal P-glycoprotein (mdr1) in interpatient variation in the oral bioavailability of cyclosporine. *Clin Pharmacol Ther* (1997) 62:248-60
- 24) Edwards DJ, Fitzsimmons ME, Schuetz EG, Yasuda K, Ducharme MP, Warbasse LH, Woster PM, Schuetz JD, Watkins P: 6',7'-Dihydroxybergamottin in grapefruit juice and Seville orange juice: effects on cyclosporine disposition, enterocyte CYP3A4, and P-glycoprotein. *Clin Pharmacol Ther* (1999) 65:237-44
- 25) Becquemont L, Verstuyft C, Kerb R, Brinkmann U, Lebot M, Jaillon P, Funck Brentano C: Effect of grapefruit juice on digoxin pharmacokinetics in humans. *Clin Pharmacol Ther* (2001) 70:311-6
- 26) Takanaga H, Ohnishi A, Matsuo H, Sawada Y: Inhibition of vinblastine efflux mediated by P-glycoprotein by grapefruit juice components in caco-2 cells. *Biol Pharm Bull* (1998) 21:1062-6

- 27) Xu J, Go ML, Lim LY: Modulation of digoxin transport across Caco-2 cell monolayers by citrus fruit juices: lime, lemon, grapefruit, and pummelo. *Pharm Res* (2003) 20:169-76
- 28) Dresser GK, Bailey DG, Leake BF, Schwarz UI, Dawson PA, Freeman DJ, Kim RB: Fruit juices inhibit organic anion transporting polypeptide-mediated drug uptake to decrease the oral availability of fexofenadine. *Clin Pharmacol Ther* (2002) 71:11-20
- 29) Lilja JJ, Backman JT, Laitila J, Luurila H, Neuvonen PJ: Itraconazole increases but grapefruit juice greatly decreases plasma concentrations of celiprolol. *Clin Pharmacol Ther* (2003) 73:192-8
- 30) Kivisto KT, Lamberg TS, Neuvonen PJ: Interactions of buspirone with itraconazole and rifampicin: effects on the pharmacokinetics of the active 1-(2-pyrimidinyl)-piperazine metabolite of buspirone. *Pharmacol Toxicol* (1999) 84:94-7
- 31) Lilja JJ, Kivisto KT, Backman JT, Lamberg TS, Neuvonen PJ: Grapefruit juice substantially increases plasma concentrations of buspirone. *Clin Pharmacol Ther* (1998) 64:655-60
- 32) Kantola T, Kivisto KT, Neuvonen PJ: Grapefruit juice greatly increases serum concentrations of lovastatin and lovastatin acid. *Clin Pharmacol Ther* (1998) 63:397-402
- 33) Lilja JJ, Kivisto KT, Neuvonen PJ.: Grapefruit juice-simvastatin interaction: effect on serum concentrations of simvastatin, simvastatin acid, and HMG-CoA reductase inhibitors. *Clin Pharmacol Ther.* (1998) 64:477-83
- 34) Lilja JJ, Kivisto KT, Neuvonen PJ.: Grapefruit juice increases serum concentrations of atorvastatin and has no effect on pravastatin. *Clin Pharmacol Ther.* (1999) 66:118-27
- 35) Di Marco MP, Edwards DJ, Wainer IW, Ducharme MP: The effect of grapefruit juice and seville orange juice on the pharmacokinetics of dextromethorphan: the role of gut CYP3A and P-glycoprotein. *Life Sci* (2002) 71:1149-60
- 36) Willner K: Excretion and decomposition of 3-methoxy-N-methylmorphinan and its demethylated derivatives in man [in German] *Arzneimittelforschung* (1963) 13:26-9
- 37) Libersa CC, Brique SA, Motte KB, Caron JF, Guedon Moreau LM, Humbert L, Vincent A, Devos P, Lhermitte MA: Dramatic inhibition of amiodarone metabolism induced by grapefruit juice. *Br J Clin*

- Pharmacol (2000) 49:373-8
- 38) Talajic M, DeRoode MR, Nattel S: Comparative electrophysiologic effects of intravenous amiodarone and desethylamiodarone in dogs: evidence for clinically relevant activity of the metabolite. *Circulation* (1987) 75:265-71
- 39) Zhou L, Chen BP, Kluger J, Fan C, Chow MS: Effects of amiodarone and its active metabolite desethylamiodarone on the ventricular defibrillation threshold. *J Am Coll Cardiol* (1998) 31:1672-8
- 40) van Agtmael MA, Gupta V, van der Graaf CA, van Boxtel CJ: The effect of grapefruit juice on the time-dependent decline of artemether plasma levels in healthy subjects. *Clin Pharmacol Ther* (1999) 66:408-14
- 41) Charbit B, Becquemont L, Lepere B, Peytavin G, Funck Brentano C: Pharmacokinetic and pharmacodynamic interaction between grapefruit juice and halofantrine. *Clin Pharmacol Ther* (2002) 72:514-23
- 42) Ku YM, Min DI, Flanigan M: Effect of grapefruit juice on the pharmacokinetics of microemulsion cyclosporine and its metabolite in healthy volunteers: does the formulation difference matter? *J Clin Pharmacol* (1998) 38:959-65
- 43) Brunner LJ, Pai KS, Munar MY, Lande MB, Olyaei AJ, Mowry JA: Effect of grapefruit juice on cyclosporin A pharmacokinetics in pediatric renal transplant patients. *Pediatr Transplant* (2000) 4:313-21
- 44) Hermann M, Asberg A, Reubsaet JL, Sather S, Berg KJ, Christensen H: Intake of grapefruit juice alters the metabolic pattern of cyclosporin A in renal transplant recipients. *Int J Clin Pharmacol Ther* (2002) 40:451-6
- 45) Penzak SR, Gubbins PO, Gurley BJ, Wang PL, Saccente M: Grapefruit juice decreases the systemic availability of itraconazole capsules in healthy volunteers. *Ther Drug Monit* (1999) 21:304-9
- 46) Malhotra S, Bailey DG, Paine MF, Watkins PB: Seville orange juice-felodipine interaction: comparison with dilute grapefruit juice and involvement of furocoumarins. *Clin Pharmacol Ther* (2001) 69:14-23
- 47) Backman JT, Maenpaa J, Belle DJ, Wrighton SA, Kivisto KT, Neuvonen PJ: Lack of correlation between in vitro and in vivo studies on the effects of tangeretin and tangerine juice on midazolam hydroxylation. *Clin Pharmacol Ther* (2000) 67:382-90
- 48) Kuhnau J: The flavonoids. A class of semi-essential food components: their role in human nutrition.

- World Rev Nutr Diet (1976)  
24:117-91
- 49) Cheng KJ, Krishnamurty HG,  
Jones GA, Simpson FJ:  
Identification of products produced  
by the anaerobic degradation of  
naringin by *Butyrivibrio* sp. C3.  
*Can J Microbiol* (1971) 17:129-31
- 50) Fuhr U, Kummert AL: The fate of  
naringin in humans: a key to  
grapefruit juice-drug interactions?  
*Clin Pharmacol Ther* (1995)  
58:365-73
- 51) Bailey DG, Munoz C, Arnold JMO,  
Strong HA, Spence JD.: Grapefruit  
juice and naringin interaction with  
nitrendipine. *Clin Pharmacol Ther*  
(1992) 51:156
- 52) Bailey DG, Arnold JM, Munoz C,  
Spence JD.: Grapefruit  
juice–felodipine interaction:  
mechanism, predictability, and  
effect of naringin. *Clin Pharmacol  
Ther.* (1993) 53:637-42
- 53) Bailey DG, Arnold JM, Strong HA,  
Munoz C, Spence JD.: Effect of  
grapefruit juice and naringin on  
nisoldipine pharmacokinetics. *Clin  
Pharmacol Ther.* (1993) 54:589-94
- 54) Eagling VA, Profit L, Back DJ:  
Inhibition of the CYP3A4-mediated  
metabolism and  
P-glycoprotein-mediated transport  
of the HIV-1 protease inhibitor  
saquinavir by grapefruit juice  
components. *Br J Clin Pharmacol*  
(1999) 48:543-52
- 55) Guo LQ, Fukuda K, Ohta T,  
Yamazoe Y: Role of  
furanocoumarin derivatives on  
grapefruit juice-mediated inhibition  
of human CYP3A activity. *Drug  
Metab Dispos* (2000) 28:766-71
- 56) Ikegawa T, Ushigome F, Koyabu N,  
Morimoto S, Shoyama Y, Naito M,  
Tsuruo T, Ohtani H, Sawada Y:  
Inhibition of P-glycoprotein by  
orange juice components,  
polymethoxyflavones in  
adriamycin-resistant human  
myelogenous leukemia  
(K562/ADM) cells. *Cancer Lett*  
(2000) 160:21-8
- 57) Ohnishi A, Matsuo H, Yamada S,  
Takanaga H, Morimoto S,  
Shoyama Y, Ohtani H, Sawada Y:  
Effect of furanocoumarin  
derivatives in grapefruit juice on the  
uptake of vinblastine by Caco-2  
cells and on the activity of  
cytochrome P450 3A4. *Br J  
Pharmacol* (2000) 130:1369-77
- 58) Takanaga H, Ohnishi A, Yamada S,  
Matsuo H, Morimoto S, Shoyama Y,  
Ohtani H, Sawada Y:  
Polymethoxylated flavones in  
orange juice are inhibitors of  
P-glycoprotein but not cytochrome  
P450 3A4. *J Pharmacol Exp Ther*  
(2000) 293:230-6
- 59) Manthey JA, Grohmann K: Phenols  
in citrus peel byproducts.

- Concentrations of hydroxycinnamates and polymethoxylated flavones in citrus peel molasses. *J Agric Food Chem* (2001) 49:3268-73
- 60) Williams D, Feely J.: Pharmacokinetic-pharmacodynamic drug interactions with HMG-CoA reductase inhibitors. *Clin Pharmacokinet.* (2002) 41:343-70
- 61) Fujino H, Yamada I, Shimada S, Nagao T, Yoneda M.: Metabolic fate of pitavastatin (NK-104), a new inhibitor of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase. Effects on drug-metabolizing systems in rats and humans. *Arzneimittelforschung.* (2002) 52:745-53
- 62) Kajinami K, Takekoshi N, Saito Y.: Pitavastatin: efficacy and safety profiles of a novel synthetic HMG-CoA reductase inhibitor. *Cardiovasc Drug Rev.* (2003) 21:199-215
- 63) Neuvonen PJ, Kantola T, Kivisto KT.: Simvastatin but not pravastatin is very susceptible to interaction with the CYP3A4 inhibitor itraconazole. *Clin Pharmacol Ther.* (1998) 63:332-41
- 64) Lee AJ, Maddix DS.: Rhabdomyolysis secondary to a drug interaction between simvastatin and clarithromycin. *Ann Pharmacother.* (2001) 35:26-31
- 65) Kantola T, Kivisto KT, Neuvonen PJ.: Erythromycin and verapamil considerably increase serum simvastatin and simvastatin acid concentrations. *Clin Pharmacol Ther.* (1998) 64:177-82
- 66) Fichtenbaum CJ, Gerber JG, Rosenkranz SL, Segal Y, Aberg JA, Blaschke T, Alston B, Fang F, Kosel B, Aweeka F.: Pharmacokinetic interactions between protease inhibitors and statins in HIV seronegative volunteers: ACTG Study A5047. *AIDS.* (2002) 16:569-77
- 67) Hsyu PH, Schultz-Smith MD, Lillibridge JH, Lewis RH, Kerr BM.: Pharmacokinetic interactions between nelfinavir and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors atorvastatin and simvastatin. *Antimicrob Agents Chemother.* (2001) 45:3445-50
- 68) Ichimaru N, Takahara S, Kokado Y, Wang JD, Hatori M, Kameoka H, Inoue T, Okuyama A.: Changes in lipid metabolism and effect of simvastatin in renal transplant recipients induced by cyclosporine or tacrolimus. *Atherosclerosis.* (2001) 158:417-23
- 69) Lilja JJ, Kivisto KT, Neuvonen PJ.: Duration of effect of grapefruit juice

- on the pharmacokinetics of the CYP3A4 substrate simvastatin. *Clin Pharmacol Ther.* (2000) 68:384-90
- 70) Kantola T, Kivisto KT, Neuvonen PJ.: Effect of itraconazole on the pharmacokinetics of atorvastatin. *Clin Pharmacol Ther.* (1998) 64:58-65
- 71) Amsden GW, Kuye O, Wei GC.: A study of the interaction potential of azithromycin and clarithromycin with atorvastatin in healthy volunteers. *J Clin Pharmacol.* (2002) 42:444-9
- 72) Siedlik PH, Olson SC, Yang BB, Stern RH.: Erythromycin coadministration increases plasma atorvastatin concentrations. *J Clin Pharmacol.* (1999) 39:501-4
- 73) Boyd RA, Stern RH, Stewart BH, Wu X, Reyner EL, Zegarac EA, Randinitis EJ, Whitfield L.: Atorvastatin coadministration may increase digoxin concentrations by inhibition of intestinal P-glycoprotein-mediated secretion. *J Clin Pharmacol.* (2000) 40:91-8
- 74) Asberg A, Hartmann A, Fjeldsa E, Bergan S, Holdaas H.: Bilateral pharmacokinetic interaction between cyclosporine A and atorvastatin in renal transplant recipients. *Am J Transplant.* (2001) 1:382-6
- 75) Kivisto KT, Kantola T, Neuvonen PJ.: Different effects of itraconazole on the pharmacokinetics of fluvastatin and lovastatin. *Br J Clin Pharmacol.* (1998) 46:49-53
- 76) Kantola T, Backman JT, Niemi M, Kivisto KT, Neuvonen PJ.: Effect of fluconazole on plasma fluvastatin and pravastatin concentrations. *Eur J Clin Pharmacol.* (2000) 56:225-9
- 77) Scripture CD, Pieper JA.: Clinical pharmacokinetics of fluvastatin. *Clin Pharmacokinet.* (2001) 40:263-81
- 78) Goldberg R, Roth D.: Evaluation of fluvastatin in the treatment of hypercholesterolemia in renal transplant recipients taking cyclosporine. *Transplantation.* (1996) 62:1559-64
- 79) Park JW, Siekmeier R, Latke P, Merz M, Mix C, Schuler S, Jaross W.: Pharmacokinetics and pharmacodynamics of fluvastatin in heart transplant recipients taking cyclosporine A. *J Cardiovasc Pharmacol Ther.* (2001) 6:351-61
- 80) Spence JD, Munoz CE, Hendricks L, Latchinian L, Khouri HE.: Pharmacokinetics of the combination of fluvastatin and gemfibrozil. *Am J Cardiol.* (1995) 76:80A-83A
- 81) Jokubaitis LA.: Development and pharmacology of fluvastatin. *Br J*

- Clin Pract Suppl. (1996) 77A:11-5
- 82) Andersson TB, Bredberg E, Ericsson H, Sjöberg H.: An evaluation of the in vitro metabolism data for predicting the clearance and drug-drug interaction potential of cyp2c9 substrates. *Drug Metab Dispos.* (2004) 32:715-21
- 83) Appel S, Rufenacht T, Kalafsky G, Tetzloff W, Kallay Z, Hitzenberger G, Kutz K.: Lack of interaction between fluvastatin and oral hypoglycemic agents in healthy subjects and in patients with non-insulin-dependent diabetes mellitus. *Am J Cardiol.* (1995) 76:29A-32A
- 84) Deslypere JP.: Clinical implications of the biopharmaceutical properties of fluvastatin. *Am J Cardiol.* (1994) 73:12D-17D
- 85) Smith HT, Jokubaitis LA, Troendle AJ, Hwang DS, Robinson WT.: Pharmacokinetics of fluvastatin and specific drug interactions. *Am J Hypertens.* (1993) 6 (11 Pt 2):375S-382S
- 86) Garnett WR, Venitz J, Wilkens RC, Dimenna G.: Pharmacokinetic effects of fluvastatin in patients chronically receiving digoxin. *Am J Med.* (1994) 96:84S-86S
- 87) Mazzu AL, Lasseter KC, Shamblen EC, Agarwal V, Lettieri J, Sundaresen P.: Itraconazole alters the pharmacokinetics of atorvastatin to a greater extent than either cerivastatin or pravastatin. *Clin. Pharmacol. Ther.*, (2000) :68,391-400
- 88) Olbricht C, Wanner C, Eisenhauer T, Kliem V, Doll R, Boddaert M, O'Grady P, Krekler M, Mangold B, Christians U.: Accumulation of lovastatin, but not pravastatin, in the blood of cyclosporine-treated kidney graft patients after multiple doses. *Clin Pharmacol Ther.* (1997) 62:311-21
- 89) Park JW, Siekmeier R, Merz M, Krell B, Harder S, Marz W, Seidel D, Schuler S, Gross W.: Pharmacokinetics of pravastatin in heart-transplant patients taking cyclosporin A. *Int J Clin Pharmacol Ther.* (2002) 40:439-50
- 90) Pan WJ, Gustavson LE, Achari R, Rieser MJ, Ye X, Gutterman C, Wallin BA.: Lack of a clinically significant pharmacokinetic interaction between fenofibrate and pravastatin in healthy volunteers. *J Clin Pharmacol.* (2000) 40:316-23
- 91) Kyrklund C, Backman JT, Neuvonen M, Neuvonen PJ.: Gemfibrozil increases plasma pravastatin concentrations and reduces pravastatin renal clearance. *Clin Pharmacol Ther.* (2003) 73:538-44
- 92) Kyrklund C, Backman JT,

- Neuvonen M, Neuvonen PJ.: Effect of rifampicin on pravastatin pharmacokinetics in healthy subjects. *Br J Clin Pharmacol.* (2004) 57:181-7
- 93) Azie NE, Brater DC, Becker PA, Jones DR, Hall SD.: The interaction of diltiazem with lovastatin and pravastatin. *Clin Pharmacol Ther.* (1998) 64:369-77
- 94) Becquemont L, Funck-Brentano C, Jaillon P.: Mibefradil, a potent CYP3A inhibitor, does not alter pravastatin pharmacokinetics. *Fundam Clin Pharmacol.* (1999) 13:232-6
- 95) Pan HY, Triscari J, DeVault AR, Smith SA, Wang-Iverson D, Swanson BN, Willard DA.: Pharmacokinetic interaction between propranolol and the HMG-CoA reductase inhibitors pravastatin and lovastatin. *Br J Clin Pharmacol.* (1991) 31:665-70
- 96) Garnett WR.: Interactions with hydroxymethylglutaryl-coenzyme A reductase inhibitors. *Am J Health Syst Pharm.* (1995) 52:1639-45
- 97) Fukazawa I, Uchida N, Uchida E, Yasuhara H.: Effects of grapefruit juice on pharmacokinetics of atorvastatin and pravastatin in Japanese. *Br J Clin Pharmacol.* (2004) 57:448-55
- 98) 蓮沼智子、中村正彦、矢地孝、有沢紀子、福島邦昭、飯島肇、齋藤康: 新規HMG-CoA還元酵素阻害薬ピタバスタチン(NK-104)の薬物間相互作用 シクロスポリンのピタバスタチン血漿中濃度に及ぼす影響 *臨床医薬.* (2003) 19:381-9
- 99) 山崎裕之、藤野秀樹、金澤瑞穂、玉木太郎、佐藤文泰、鈴木幹夫、北原真樹.: 新規HMG-CoA還元酵素阻害薬ピタバスタチン(リバロ錠)の薬理及び薬物動態的特徴と臨床効果 *日本薬理学雑誌.* (2004) 123:349-61
- 100) Abernethy DR.: The pharmacokinetic profile of amlodipine. *Am Heart J.* (1989) 118:1100-3
- 101) Bailey DG, Bend JR, Arnold JM, Tran LT, Spence JD.: Erythromycin-felodipine interaction: magnitude, mechanism, and comparison with grapefruit juice. *Clin Pharmacol Ther.* (1996) 60:25-33
- 102) Liedholm H, Nordin G.: Erythromycin-felodipine interaction. *DICP.* (1991) 25:1007-8
- 103) Jalava KM, Oikola KT, Neuvonen PJ.: Itraconazole greatly increases plasma concentrations and effects of felodipine. *Clin Pharmacol Ther.* (1997) 61:410-5
- 104) Neuvonen PJ, Suhonen R.: Itraconazole interacts with felodipine. *J Am Acad Dermatol.* (1995) 33:134-5
- 105) Janzon K, Edgar B, Lundborg P, Regardh CG.: The influence of



- cimetidine and spinolactone on the pharmacokinetics and haemodynamics effects of felodipine in healthy subjects. *Acta Pharmacol Toxicol.* (1986) 59 Suppl 5: 98
- 106) Edgar B, Lundborg P, Regardh CG.: Clinical pharmacokinetics of felodipine. A summary. *Drugs.* (1987) 34 Suppl 3:16-27
- 107) Tailor SA, Gupta AK, Walker SE, Shear NH.: Peripheral edema due to nifedipine-itraconazole interaction: a case report. *Arch Dermatol.* (1996) 132:350-2
- 108) Smith SR, Kendall MJ, Lobo J, Beerah A, Jack DB, Wilkins MR.: Ranitidine and cimetidine; drug interactions with single dose and steady-state nifedipine administration. *Br J Clin Pharmacol.* (1987) 23:311-5
- 109) Kirch W, Janisch HD, Heidemann H, Ramsch K, Ohnhaus EE.: Effect of cimetidine and ranitidine on the pharmacokinetics and anti-hypertensive effect of nifedipine. [Article in German] *Dtsch Med Wochenschr.* (1983) 108:1757-61
- 110) Kirch W, Ramsch K, Janisch HD, Ohnhaus EE.: The influence of two histamine H<sub>2</sub>-receptor antagonists, cimetidine and ranitidine, on the plasma levels and clinical effect of nifedipine and metoprolol. *Arch Toxicol Suppl.* (1984) 7: 256-9
- 111) Renwick AG, Le Vie J, Challenor VF, Waller DG, Gruchy B, George CF.: Factors affecting the pharmacokinetics of nifedipine. *Eur J Clin Pharmacol.* (1987) 32:351-5
- 112) Khan A, Langley SJ, Mullins FG, Dixon JS, Toon S.: The pharmacokinetics and pharmacodynamics of nifedipine at steady state during concomitant administration of cimetidine or high dose ranitidine. *Br J Clin Pharmacol.* (1991) 32:519-22
- 113) Schwartz JB, Upton RA, Lin ET, Williams RL, Benet LZ.: Effect of cimetidine or ranitidine administration on nifedipine pharmacokinetics and pharmacodynamics. *Clin Pharmacol Ther.* (1988) 43:673-80
- 114) Heinig R.: Clinical pharmacokinetics of nisoldipine coat-core. *Clin Pharmacokinet.* (1998) 35:191-208
- 115) van Harten J, van Brummelen P, Lodewijks MT, Danhof M, Breimer DD.: Pharmacokinetics and hemodynamic effects of nisoldipine and its interaction with cimetidine. *Clin Pharmacol Ther.* (1988) 43:332-41
- 116) Muck W, Wingender W, Seiberling M, Woelke E, Ramsch KD, Kuhlmann J.: Influence of the

- H<sub>2</sub>-receptor antagonists cimetidine and ranitidine on the pharmacokinetics of nimodipine in healthy volunteers. *Eur J Clin Pharmacol.* (1992) 42:325-8
- 117) Muck W, Ahr G, Kuhlmann J.: Nimodipine. Potential for drug-drug interactions in the elderly. *Drugs Aging.* (1995) 6:229-42
- 118) Barchielli M, Dolfini E, Farina P.: Clinical pharmacokinetics of lercanidipine. *J Cardiovasc Pharmacol.* (1997) : 29 Suppl 2: S1
- 119) Kirch W, Hutt HJ, Heidemann H, Ramsch K, Janisch HD, Ohnhaus EE.: Drug interactions with nitrendipine. *J Cardiovasc Pharmacol.* (1984) 6 Suppl 7:S982-5
- 120) Soons PA, Vogels BA, Roosemalen MC, Schoemaker HC, Uchida E, Edgar B, Lundahl J, Cohen AF, Breimer DD: Grapefruit juice and cimetidine inhibit stereoselective metabolism of nitrendipine in humans. *Clin Pharmacol Ther* (1991) 50:394-403
- 121) Wing LM, Miners JO, Lillywhite KJ.: Verapamil disposition—effects of sulphinpyrazone and cimetidine. *Br J Clin Pharmacol.* (1985) 19:385-91
- 122) Abernethy DR, Schwartz JB, Todd EL.: Lack of interaction between verapamil and cimetidine. *Clin Pharmacol Ther.* (1985) 38:342-9
- 123) Smith MS, Benyunes MC, Bjornsson TD, Shand DG, Pritchett EL.: Influence of cimetidine on verapamil kinetics and dynamics. *Clin Pharmacol Ther.* (1984) 36:551-4
- 124) Loi CM, Rollins DE, Dukes GE, Peat MA.: Effect of cimetidine on verapamil disposition. *Clin Pharmacol Ther.* (1985) 37:654-7
- 125) Mikus G, Eichelbaum M, Fischer C, Gumulka S, Klotz U, Kroemer HK.: Interaction of verapamil and cimetidine: stereochemical aspects of drug metabolism, drug disposition and drug action. *J Pharmacol Exp Ther.* (1990) 253:1042-8
- 126) Winship LC, McKenney JM, Wright JT Jr, Wood JH, Goodman RP.: The effect of ranitidine and cimetidine on single-dose diltiazem pharmacokinetics. *Pharmacotherapy.* (1985) 5:16-9
- 127) Vincent J, Harris SI, Foulds G, Dogolo LC, Willavize S, Friedman HL.: Lack of effect of grapefruit juice on the pharmacokinetics and pharmacodynamics of amlodipine. *Br J Clin Pharmacol.* (2000) 50:455-63
- 128) Josefsson M, Zackrisson AL, Ahlner J: Effect of grapefruit juice on the pharmacokinetics of amlodipine in healthy volunteers. *Eur J Clin Pharmacol* (1996)

- 51:189-93
- 129) Bailey DG, Arnold JM, Bend JR, Tran LT, Spence JD.: Grapefruit juice-felodipine interaction: reproducibility and characterization with the extended release drug formulation. *Br J Clin Pharmacol.* (1995) 40:135-40
- 130) Lundahl J, Regardh CG, Edgar B, Johnsson G.: Effects of grapefruit juice ingestion—pharmacokinetics and haemodynamics of intravenously and orally administered felodipine in healthy men. *Eur J Clin Pharmacol.* (1997) 52:139-45
- 131) Lundahl JU, Regardh CG, Edgar B, Johnsson G.: The interaction effect of grapefruit juice is maximal after the first glass. *Eur J Clin Pharmacol.* (1998) 54:75-81
- 132) Edgar B, Bailey D, Bergstrand R, Johnsson G, Regardh CG: Acute effects of drinking grapefruit juice on the pharmacokinetics and dynamics of felodipine—and its potential clinical relevance. *Eur J Clin Pharmacol* (1992) 42:313-7
- 133) Dresser GK, Bailey DG, Carruthers SG.: Grapefruit juice—felodipine interaction in the elderly. *Clin Pharmacol Ther.* (2000) 68:28-34
- 134) Uno T, Ohkubo T, Sugawara K, Higashiyama A, Motomura S, Ishizaki T: Effects of grapefruit juice on the stereoselective disposition of nicardipine in humans: evidence for dominant presystemic elimination at the gut site. *Eur J Clin Pharmacol* (2000) 56:643-9
- 135) Sigusch H, Hippus M, Henschel L, Kaufmann K, Hoffmann A: Influence of grapefruit juice on the pharmacokinetics of a slow release nifedipine formulation. *Pharmazie* (1994) 49:522-4
- 136) Takanaga H, Ohnishi A, Murakami H, Matsuo H, Higuchi S, Urae A, Irie S, Furuie H, Matsukuma K, Kimura M, Kawano K, Orii Y, Tanaka T, Sawada Y: Relationship between time after intake of grapefruit juice and the effect on pharmacokinetics and pharmacodynamics of nisoldipine in healthy subjects. *Clin Pharmacol Ther* (2000) 67:201-14
- 137) Fuhr U, Maier Bruggemann A, Blume H, Muck W, Unger S, Kuhlmann J, Huschka C, Zaigler M, Rietbrock S, Staib AH: Grapefruit juice increases oral nimodipine bioavailability. *Int J Clin Pharmacol Ther* (1998) 36:126-32
- 138) Klotz U.: Interaction potential of lercanidipine, a new vasoselective dihydropyridine calcium antagonist. *Arzneimittelforschung.* (2002) 52:155-61
- 139) 矢島洋一、飯島肇、横山鍊藏: Ca拮抗薬塩酸エホニジピン(ランデル錠)

- の薬物動態に及ぼすグレープフルーツジュースの影響 薬理と治療. (2003) 31:579-88
- 140) Fuhr U, Muller Peltzer H, Kern R, Lopez Rojas P, Junemann M, Harder S, Staib AH: Effects of grapefruit juice and smoking on verapamil concentrations in steady state. *Eur J Clin Pharmacol* (2002) 58:45-53
- 141) Fuhr U, Harder S, Lopez-Rojas P, Muller-Peltzer H, Kern R, Staib H.: Increase of verapamil concentrations in steady state by coadministration of grapefruit juice. *Naunyn Schmiedebergs Arch Pharmacol.* (1994) 349: R134
- 142) Zaidenstein R, Dishy V, Gips M, Soback S, Cohen N, Weissgarten J, Blatt A, Golik A.: The effect of grapefruit juice on the pharmacokinetics of orally administered verapamil. *Eur J Clin Pharmacol.* (1998) 54:337-40
- 143) Sigusch H, Henschel L, Kraul H, Merkel U, Hoffmann A.: Lack of effect of grapefruit juice on diltiazem bioavailability in normal subjects. *Pharmazie.* (1994) 49:675-9
- 144) Christensen H, Asberg A, Holmboe AB, Berg KJ: Coadministration of grapefruit juice increases systemic exposure of diltiazem in healthy volunteers. *Eur J Clin Pharmacol* (2002) 58:515-20
- 145) Schwartz JB.: Effects of amlodipine on steady-state digoxin concentrations and renal digoxin clearance. *J Cardiovasc Pharmacol.* (1988) 12:1-5
- 146) Rehnqvist N, Billing E, Moberg L, Lundman T, Olsson G.: Pharmacokinetics of felodipine and effect on digoxin plasma levels in patients with heart failure. *Drugs.* (1987) 34 Suppl 3:33-42
- 147) Dunselman PH, Scaf AH, Kuntze CE, Lie KI, Wesseling H.: Digoxin-felodipine interaction in patients with congestive heart failure. *Eur J Clin Pharmacol.* (1988) 35:461-5
- 148) Lessem J, Bellineto A.: Interaction between digoxin and the calcium antagonists nifedipine and tiapamil. *Clin Ther.* (1983) 5:595-602
- 149) Debruyne D, Commeau P, Grollier G, Huret B, Scanu P, Moulin M.: Nifedipine does not significantly affect serum digoxin concentrations at the steady state of patients with congestive heart failure. *Int J Clin Pharmacol Res.* (1989) 9:15-9
- 150) Kirch W, Hutt HJ, Dylewicz P, Graf KJ, Ohnhaus EE.: Dose-dependence of the nifedipine-digoxin interaction? *Clin Pharmacol Ther.* (1986) 39: 35-9
- 151) Belz GG, Doering W, Munkes R,

- Matthews J.: Interaction between digoxin and calcium antagonists and antiarrhythmic drugs. *Clin Pharmacol Ther.* (1983) 33:410-7
- 152) Kirch W, Stenzel J, Dylewicz P, Hutt HJ, Santos SR, Ohnhaus EE.: Influence of nisoldipine on haemodynamic effects and plasma levels of digoxin. *Br J Clin Pharmacol.* (1986) 22:155-9
- 153) Abernethy DR, Schwartz JB.: Pharmacokinetics of calcium antagonists under development. *Clin Pharmacokinet.* (1988) 15:1-14
- 154) Rodin SM, Johnson BF, Wilson J, Ritchie P, Johnson J.: Comparative effects of verapamil and isradipine on steady-state digoxin kinetics. *Clin Pharmacol Ther.* (1988) 43: 668-72
- 155) Beudeker HJ, van der Velden JW, van der Aar EM.: Interaction profile and tolerability of barnidipine. *Int J Clin Pract Suppl.* (2000):114: 36-40
- 156) von Nieciecki A, Huber HJ, Stanislaus F.: Pharmacokinetics of nilvadipine. *J Cardiovasc Pharmacol.* (1992) 20 Suppl 6:S22-9
- 157) Kirch W, Logemann C, Heidemann H, Santos SR, Ohnhaus EE.: Nitrendipine/digoxin interaction. *J Cardiovasc Pharmacol.* 10 (1987) 10 Suppl 10 :S74-5
- 158) Pedersen KE, Thayssen P, Klitgaard NA, Christiansen BD, Nielsen-Kudsk F.: Influence of verapamil on the inotropism and pharmacokinetics of digoxin. *Eur J Clin Pharmacol.* (1983) 25:199-206
- 159) Rameis H, Magometschnigg D, Ganzinger U.: The diltiazem-digoxin interaction. *Clin Pharmacol Ther.* (1984) 36: 183-9
- 160) Elkayam U, Parikh K, Torkan B, Weber L, Cohen JL, Rahimtoola SH.: Effect of diltiazem on renal clearance and serum concentration of digoxin in patients with cardiac disease. *Am J Cardiol.* (1985) 55:1393-5
- 161) Yoshida A, Fujita M, Kurosawa N, Nioka M, Shichinohe T, Arakawa M, Fukuda R, Owada E, Ito K.: Effects of diltiazem on plasma level and urinary excretion of digoxin in healthy subjects. *Clin Pharmacol Ther.* (1984) 35:681-5
- 162) 平山武司、常田愛子、黒山政一、矢後和夫: HMG - CoA還元酵素阻害薬pravastatin sodium 後発医薬品の医薬品添付文書における薬物動態情報のあり方に関する研究 *医療薬学.* (2004) 30:770-6
- 163) 中村敏明、福岡美紀、萱野勇一郎、後藤伸之、脇屋義文、政田幹夫: 後発医薬品の生物学的同等性試験における試験間差 *医療薬学.* (2005) 31: 158-63
- 164) Williams D, Feely J.:

- Pharmacokinetic-pharmacodynamic drug interactions with HMG-CoA reductase inhibitors. *Clin Pharmacokinet.* (2002) 41:343-70
- 165) Arnadóttir M, Eriksson LO, Thysell H, Karkas JD.: Plasma concentration profiles of simvastatin 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitory activity in kidney transplant recipients with and without ciclosporin. *Nephron.* (1993) 65:410-3
- 166) Campana C, Iacona I, Regazzi MB, Gavazzi A, Perani G, Raddato V, Montemartini C, Viganò M.: Efficacy and pharmacokinetics of simvastatin in heart transplant recipients. *Ann Pharmacother.* (1995) 29:235-9
- 167) Kanathur N, Mathai MG, Byrd RP Jr, Fields CL, Roy TM.: Simvastatin-diltiazem drug interaction resulting in rhabdomyolysis and hepatitis. *Tenn Med.* (2001) 94:339-41
- 168) Lilja JJ, Neuvonen M, Neuvonen PJ.: Effects of regular consumption of grapefruit juice on the pharmacokinetics of simvastatin. *Br J Clin Pharmacol.* (2004) 58:56-60
- 169) Todd PA, Goa KL.: Simvastatin. A review of its pharmacological properties and therapeutic potential in hypercholesterolaemia. *Drugs.* (1990) 40:583-607
- 170) Asberg A.: Interactions between cyclosporin and lipid-lowering drugs: implications for organ transplant recipients. *Drugs.* (2003) 63:367-78
- 171) Hsiang B, Zhu Y, Wang Z, Wu Y, Sasseville V, Yang WP, Kirchgessner TG.: A novel human hepatic organic anion transporting polypeptide (OATP2). Identification of a liver-specific human organic anion transporting polypeptide and identification of rat and human hydroxymethylglutaryl-CoA reductase inhibitor transporters. *J Biol Chem.* (1999) 274:37161-8
- 172) Shitara Y, Itoh T, Sato H, Li AP, Sugiyama Y.: Inhibition of transporter-mediated hepatic uptake as a mechanism for drug-drug interaction between cerivastatin and cyclosporin A. *J Pharmacol Exp Ther.* (2003) 304:610-6
- 173) Bailey DG, Malcolm J, Arnold O, Spence JD.: Grapefruit juice-drug interactions. *Br J Clin Pharmacol.* (1998) 46:101-10
- 174) Lin JH, Yamazaki M.: Role of P-glycoprotein in pharmacokinetics: clinical implications. *Clin Pharmacokinet.* (2003) 42:59-98
- 175) Wang E, Casciano CN, Clement RP, Johnson WW.: HMG-CoA

- reductase inhibitors (statins) characterized as direct inhibitors of P-glycoprotein. *Pharm Res.* (2001) 18:800-6
- 176) Sakaeda T, Takara K, Kakumoto M, Ohmoto N, Nakamura T, Iwaki K, Tanigawara Y, Okumura K.: Simvastatin and lovastatin, but not pravastatin, interact with MDR1. *J Pharm Pharmacol.* (2002) 54:419-23
- 177) Regazzi MB, Iacona I, Campana C, Gavazzi A, Vigano M, Perani G.: Clinical efficacy and pharmacokinetics of HMG-CoA reductase inhibitors in heart transplant patients treated with cyclosporin A. *Transplant Proc.* (1994) 26:2644-5
- 178) 手術等で摘出されたヒト組織を用いた研究開発の在り方について (答申) 平成10年12月16日厚科審第13号 (1998)
- 179) 医療用医薬品添付文書の記載要領について 平成9年4月25日薬発第606号 (1997)
- 180) 医療用医薬品の使用上の注意記載要領について 平成9年4月25日薬発第607号 (1997):
- 181) 医療用医薬品添付文書の記載要領について 平成9年4月25日薬安第59号 (1997):
- 182) 非臨床薬物動態ガイドラインについて 平成10年6月26日医薬審第496号 (1998):
- 183) *Guidance for Industry: Drug Metabolism/Drug Interaction Studies in the Drug Development Process: Studies In Vitro*, FDA, CDER and CBER (1997)
- 184) *Guidance for Industry: In Vivo Drug Metabolism/Drug Interaction Studies -- Study Design, Data Analysis and Recommendations for Dosing and Labeling*, FDA, CDER and CBER (1999):
- 185) 医薬品の臨床薬物動態試験について 平成13年6月1日医薬審発第796号 (2001):
- 186) JP interaction: 薬物相互作用の検討方法について 平成13年6月4日医薬審発第813号 (2001):
- 187) Ranganna S, Govindarajan VS, Ramana KV.: Citrus fruits. Part II. Chemistry, technology, and quality evaluation. *B. Technology. Crit Rev Food Sci Nutr.* (1983) 19:1-98
- 188) Bailey DG, Arnold JM, Spence JD: Grapefruit juice and drugs. How significant is the interaction? *Clin Pharmacokinet* (1994) 26:91-8
- 189) Katoh M, Nakajima M, Shimada N, Yamazaki H, Yokoi T.: Inhibition of human cytochrome P450 enzymes by 1,4-dihydropyridine calcium antagonists: prediction of in vivo drug-drug interactions. *Eur J Clin Pharmacol.* (2000) 55:843-52
- 190) Katoh M, Nakajima M, Yamazaki H, Yokoi T.: Inhibitory potencies of 1,4-dihydropyridine calcium antagonists to

- P-glycoprotein-mediated transport: comparison with the effects on CYP3A4. *Pharm Res.* (2000) 17:1189-97
- 191) Kakumoto M, Takara K, Sakaeda T, Tanigawara Y, Kita T, Okumura K.: MDR1-mediated interaction of digoxin with antiarrhythmic or antianginal drugs. *Biol Pharm Bull.* (2002) 25:1604-7
- 192) Takara K, Kakumoto M, Tanigawara Y, Funakoshi J, Sakaeda T, Okumura K.: Interaction of digoxin with antihypertensive drugs via MDR1. *Life Sci.* (2002) 70:1491-500
- 193) 山田安彦、澤田康文、伊賀立二.: 医療用医薬品添付文書における「薬物間相互作用」欄の問題点と解決策 *月刊薬事.* (1996) 38: 803-10
- 194) 西島英利: 併用禁忌データベースの公開について *日本医師会雑誌.* (2002) 128: 460-1
- 195) 木津純子、新井あゆみ、野出忍、牧村吏恵、松下智子、脇祐子、宮崎智雄、巨勢典子、堀誠治: 医薬品添付文書等における相互作用情報 ニューキノロン系抗菌薬と非ステロイド性抗炎症薬の相互作用を中心として *医薬品情報学.* (2003) 5: A26
- 196) Thompson PD, Clarkson P, Karas RH.: Statin-associated myopathy. *JAMA.* (2003) 289:1681-90
- 197) Psaty BM, Furberg CD, Ray WA, Weiss NS.: Potential for conflict of interest in the evaluation of suspected adverse drug reactions: use of cerivastatin and risk of rhabdomyolysis. *JAMA.* (2004) 292:2622-31
- 198) Davidson MH.: Rosuvastatin safety: lessons from the FDA review and post-approval surveillance. *Expert Opin Drug Saf.* (2004) 3:547-57



Fig. 1 添付文書中にCYP分子種が記載されている医薬品

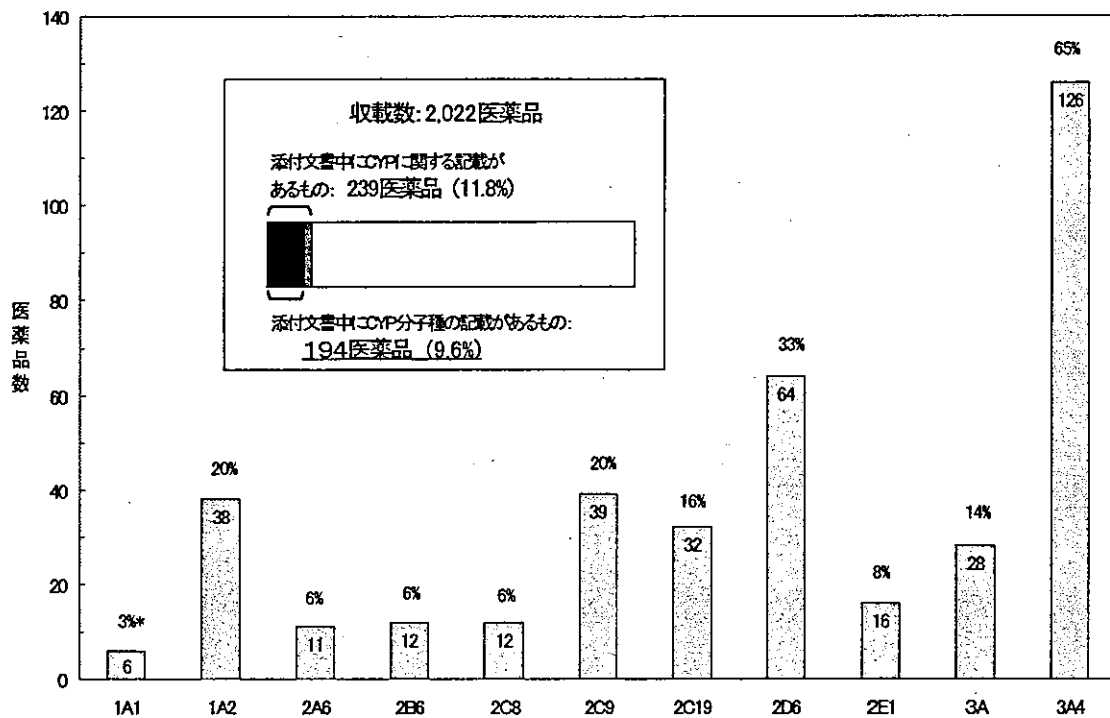
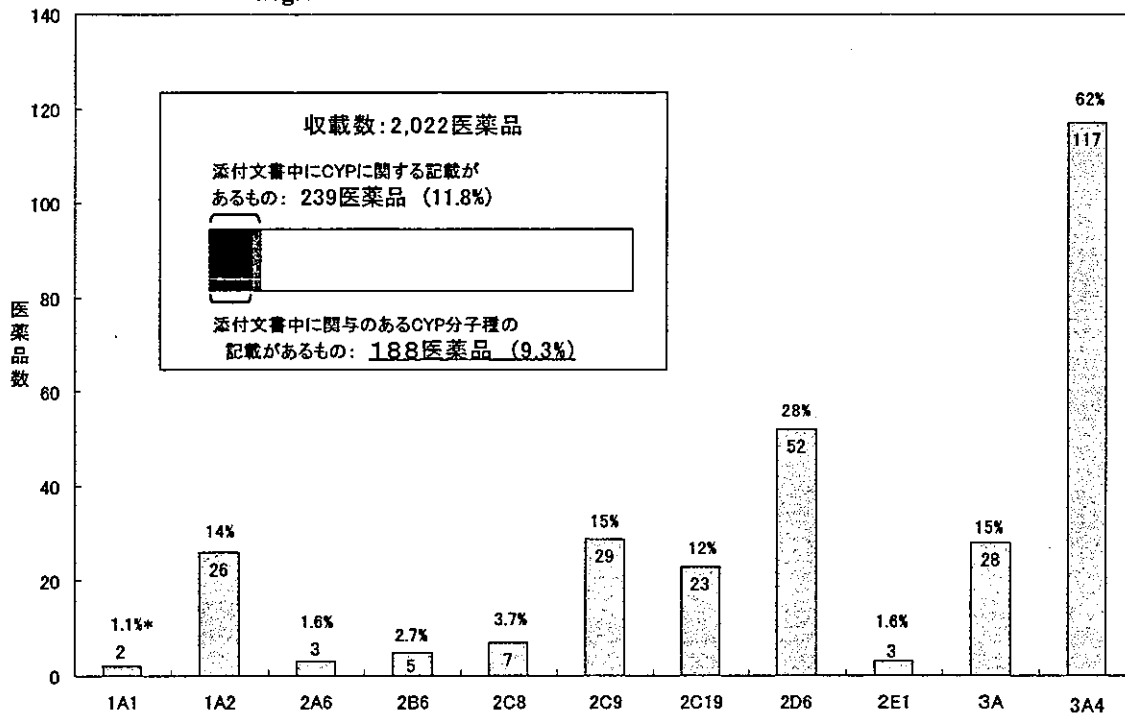


Fig. 2 添付文書中に関与のあるCYP分子種の記載がある医薬品



\*: 添付文書中に関与のあるCYP分子種の記載がある188医薬品に対する割合

Table 1, 薬効分類 (医療薬日本医薬品集第27版より)

神経系及び感覚器官用医薬品

| 大分類               | 小分類  |
|-------------------|--|
| 中枢神経系用薬           | 全身麻酔剤<br>催眠鎮静剤、抗不安剤<br>抗てんかん剤<br>解熱鎮痛消炎剤<br>興奮剤、覚せい剤<br>抗パーキンソン剤<br>精神神経用剤<br>総合感官剤<br>その他の中枢神経系用薬 |
| 末梢神経系用薬           | 局所麻酔剤<br>骨格筋弛緩剤<br>自律神経剤<br>鎮けい剤<br>発汗剤、止汗剤<br>その他の末梢神経系用薬   |
| 感覚器官用薬            | 眼科用剤<br>耳鼻科用剤<br>鎮痛剤<br>その他の感覚器官用薬   |
| その他の神経系及び感覚器官用医薬品 |  |

個々の器官系用医薬品

| 大分類                  | 小分類  |
|----------------------|--|
| 循環器官用薬               | 強心剤<br>不整脈用剤<br>利尿剤<br>血圧降下剤<br>血管補強剤<br>血管収縮剤<br>血管拡張剤<br>高脂血症用剤<br>その他の循環器官用薬  |
| 呼吸器官用薬               | 呼吸促進剤<br>鎮咳剤<br>去たん剤<br>鎮咳去たん剤<br>気管支拡張剤<br>含嗽剤<br>その他の呼吸器官用薬  |
| 消化器官用薬               | 止しゃ剤、整腸剤<br>消化性潰瘍用剤<br>健胃消化剤<br>制酸剤<br>下剤、浣腸剤<br>利胆剤<br>複合胃腸剤<br>その他の消化器官用薬  |
| ホルモン剤<br>(抗ホルモン剤を含む) | 脳下垂体ホルモン剤<br>垂腺線ホルモン剤<br>甲状腺、副甲状腺ホルモン剤<br>タンパク同化ステロイド剤<br>副腎ホルモン剤<br>男性ホルモン剤<br>卵巣ホルモン及び黄体ホルモン剤<br>混合ホルモン剤<br>その他のホルモン剤<br>(抗ホルモン剤を含む) |
| 泌尿生殖器官及び肛門用薬         | 泌尿器官用剤<br>生殖器官用剤 (性病予防剤を含む)<br>子宮収縮剤<br>避妊剤<br>痔疾用剤<br>その他の泌尿生殖器官及び肛門用薬  |
| 外皮用剤                 | 外皮用殺菌消毒剤<br>創傷保護剤<br>化膿性疾患用剤<br>鎮痛、鎮痒、取れん、消炎剤<br>寄生性皮膚疾患用剤<br>皮膚軟化剤 (腐食剤を含む)<br>毛髪用剤<br>(脱毛剤、脱毛剤、染毛剤、養毛剤)<br>浴剤<br>その他の外皮用剤            |

歯科口腔用薬

|   |
|---|
| 歯科用局所麻酔剤<br>歯髓失活剤<br>歯科用鎮痛鎮静剤<br>(根管及び歯窩消毒剤を含む)<br>歯髓乾死剤 (根管充填剤を含む)<br>歯髓覆罩剤<br>歯科用抗生物質製剤<br>その他の歯科口腔用薬 |
| その他の個々の器官系用医薬品  |

代謝性医薬品

| 大分類        | 小分類   |
|------------|---|
| ビタミン剤      | ビタミンA及びD剤<br>ビタミンB <sub>1</sub> 剤<br>ビタミンB <sub>2</sub> 剤 (ビタミンB <sub>6</sub> 剤を除く)<br>ビタミンC剤<br>ビタミンE剤<br>ビタミンK剤<br>混合ビタミン剤<br>(ビタミンA・D混合製剤を除く)<br>その他のビタミン剤 |
| 滋養強壮薬      | カルシウム剤<br>無機質製剤<br>糖類剤<br>有機酸製剤<br>蛋白質・アミノ酸製剤<br>臓器製剤<br>乳幼児用剤<br>その他の滋養強壮薬   |
| 血液・体液用薬    | 血液代用剤<br>止血剤<br>血液凝固阻止剤<br>その他の血液・体液用薬  |
| 人工透析用薬     | 人工腎臓透析用剤<br>腹膜透析用剤<br>その他の人工透析用薬  |
| その他の代謝性医薬品 | 肝臓疾患用剤<br>解毒剤<br>習慣性中毒用剤<br>痛風治療剤<br>酵素製剤<br>糖尿病用剤<br>総合代謝性製剤<br>他に分類されない代謝性医薬品   |

組織細胞機能用医薬品

| 大分類            | 小分類  |
|----------------|--|
| 細胞賦活用薬         | クロロフィル製剤<br>色素製剤<br>その他の細胞賦活用薬                         |
| 腫瘍用薬           | アルキル剤<br>代謝拮抗剤<br>抗腫瘍性抗生物質製剤<br>抗腫瘍性植物成分製剤<br>その他の腫瘍用薬 |
| 放射性医薬品         |  |
| アレルギー用薬        | 抗ヒスタミン剤<br>刺激療法剤<br>非特異性免疫原製剤<br>その他のアレルギー用薬           |
| その他の組織細胞機能用医薬品 |  |

生薬及び漢方処方に基づく医薬品

| 大分類                 | 小分類        |
|---------------------|------------|
|                     | 生薬<br>漢方製剤 |
| その他の生薬及び漢方処方に基づく医薬品 |            |

病原生物に対する医薬品

| 大分類             | 小分類  |
|-----------------|--|
| 抗生物質製剤          | 主としてグラム陽性菌に作用するもの<br>主としてグラム陰性菌に作用するもの<br>主としてグラム陽性・陰性菌に作用するもの<br>主としてグラム陽性菌、マイコプラズマに作用するもの<br>主としてグラム陽性・陰性菌、リケッチア、クラミジアに作用するもの<br>主として抗酸菌に作用するもの<br>主としてカビに作用するもの<br>その他の抗生物質製剤 (複合抗生物質製剤を含む) |
| 化学療法剤           | サルファ剤<br>抗結核剤<br>抗ハンセン病剤<br>合成抗菌剤<br>抗ウイルス剤<br>その他の化学療法剤   |
| 生物学的製剤          | ワクチン類<br>毒素及びトキソイド類<br>抗毒素類及びレプトスピラ血清類<br>血液製剤類<br>生物学的試験用製剤類<br>混合生物学的製剤<br>その他の生物学的製剤  |
| 寄生動物に対する薬       | 抗原虫薬<br>駆虫剤<br>その他の寄生動物に対する薬   |
| その他の病原生物に対する医薬品 |  |

治療を主目的としない医薬品

| 大分類               | 小分類   |
|-------------------|---|
| 調剤用薬              | 賦形剤<br>軟膏基剤<br>溶解剤<br>矯味、矯臭、着色剤<br>乳化剤<br>その他の調剤用薬  |
| 診断用薬              | 線造影剤<br>機能検査用試薬<br>その他の診断用薬   |
| 公衆衛生用薬            | 防腐剤<br>防疫用殺菌消毒剤<br>防虫剤<br>殺虫剤<br>その他の公衆衛生用薬   |
| 体外診断用医薬品          | 一般検査用試薬<br>血液検査用紙薬<br>生化学的検査用試薬<br>免疫血清学的検査用試薬<br>細菌学的検査用薬<br>病理組織検査用薬<br>体外診断用放射性医薬品<br>その他の体外診断用医薬品 |
| その他の治療を主目的としない医薬品 | 群創膏<br>他に分類されない治療を主目的としない医薬品  |

麻薬

| 大分類                 | 小分類  |
|---------------------|--|
| アルカロイド系製剤<br>(天然麻薬) | アヘンアルカロイド系製剤<br>コカアルカロイド系製剤<br>その他のアルカロイド系麻薬<br>(天然麻薬) |
| 非アルカロイド系麻薬          | 合成麻薬   |

Fig. 3 添付文書中にCYPに関する記載がある医薬品の薬効群中の割合

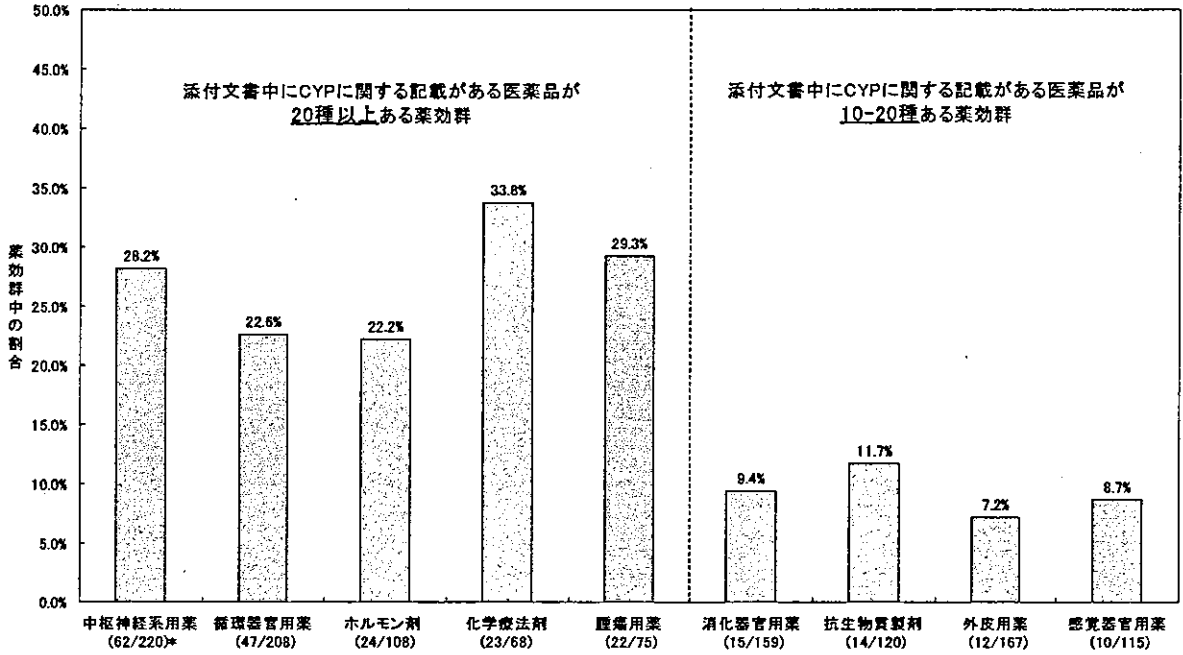


Table2 添付文書中にCYPに関する記載がある医薬品の各薬効群中の割合  
(薬効小分類)

| 薬効群                   | 添付文書中にシクロ-P450に関する記載がある医薬品 |           |              |
|-----------------------|----------------------------|-----------|--------------|
|                       | 全医薬品数                      | 医薬品数      | 薬効群中の割合      |
| <b>中枢神経系用薬</b>        | <b>220</b>                 | <b>62</b> | <b>28.2%</b> |
| 全身麻酔剤                 | 12                         | 2         | 16.7%        |
| 催眠鎮静剤、抗不安剤            | 45                         | 17        | 37.8%        |
| 抗てんかん剤                | 17                         | 9         | 52.9%        |
| 解熱鎮痛消炎剤               | 62                         | 9         | 14.5%        |
| 興奮剤、覚せい剤              | 2                          | 0         | 0.0%         |
| 抗パーキンソン剤              | 17                         | 4         | 23.5%        |
| 精神神経用剤                | 57                         | 23        | 40.4%        |
| 総合感冒剤                 | 4                          | 0         | 0.0%         |
| その他の中枢神経系用薬           | 14                         | 2         | 14.3%        |
| <b>循環器官用薬</b>         | <b>208</b>                 | <b>47</b> | <b>22.6%</b> |
| 強心剤                   | 30                         | 6         | 20.0%        |
| 不整脈用剤                 | 33                         | 16        | 48.5%        |
| 利尿剤                   | 15                         | 0         | 0.0%         |
| 血圧降下剤                 | 66                         | 17        | 25.8%        |
| 血管補強剤                 | 0                          | 0         | —            |
| 血管収縮剤                 | 7                          | 3         | 42.9%        |
| 血管拡張剤                 | 22                         | 5         | 22.7%        |
| 高脂血症用剤                | 21                         | 5         | 23.8%        |
| その他の循環器官用薬            | 28                         | 1         | 3.6%         |
| <b>ホルモン剤</b>          | <b>108</b>                 | <b>24</b> | <b>22.2%</b> |
| 脳下垂体ホルモン剤             | 8                          | 0         | 0.0%         |
| 唾液腺ホルモン剤              | 1                          | 0         | 0.0%         |
| 甲状腺、副甲状腺ホルモン剤         | 5                          | 1         | 20.0%        |
| タンパク同化ステロイド剤          | 6                          | 0         | 0.0%         |
| 副腎ホルモン剤               | 29                         | 21        | 72.4%        |
| 男性ホルモン剤               | 4                          | 0         | 0.0%         |
| 卵胞ホルモン及び黄体ホルモン剤       | 19                         | 1         | 5.3%         |
| 混合ホルモン剤               | 13                         | 1         | 7.7%         |
| その他のホルモン剤(抗ホルモン剤を含む。) | 23                         | 0         | 0.0%         |
| <b>化学療法剤</b>          | <b>68</b>                  | <b>23</b> | <b>33.8%</b> |
| サルファ剤                 | 4                          | 0         | 0.0%         |
| 抗結核剤                  | 7                          | 2         | 28.6%        |
| 抗ハンセン病剤               | 4                          | 1         | 25.0%        |
| 合成抗菌剤                 | 19                         | 2         | 10.5%        |
| 抗ウイルス剤                | 26                         | 13        | 50.0%        |
| その他の化学療法剤             | 8                          | 5         | 62.5%        |
| <b>腫瘍用薬</b>           | <b>75</b>                  | <b>22</b> | <b>29.3%</b> |
| アルキル化剤                | 10                         | 2         | 20.0%        |
| 代謝拮抗剤                 | 14                         | 3         | 21.4%        |
| 抗腫瘍性抗生物質製剤            | 13                         | 1         | 7.7%         |
| 抗腫瘍性植物成分製剤            | 9                          | 8         | 88.9%        |
| その他の腫瘍用薬              | 29                         | 8         | 27.6%        |