CURRICULUM VITAE

Neuvonen, Pertti J.
born 25 August 1943 (Kirvu, Finland),
Married, 5 children
Researcher ID: G - 4675 – 2011

Education and Training
Matriculation examination, 1962
Military Service (obligatory), 1962-3; rank, second lieutenant
Licentiate of Medicine (MD), University of Helsinki, 1970
Licensed physician, 1970
Doctor of Medical Sciences (PhD), University of Helsinki, 1971
Title of Docent ("Senior Lecturer competence") in Pharmacology, Univ. Helsinki, 1972
Specialist Degree in Clinical Pharmacology, 1977

Current Position
Emeritus Professor of Clinical Pharmacology (since 1. Sept. 2011),
Researcher, University of Helsinki, Dept. Clinical Pharmacology, 2011-

Previous Professional Appointments
University of Helsinki, Department of Pharmacology, Tutor, 1966 -1969; Lecturer 1970
Hannover Medical School, W-Germany, Fellow of A. v. Humboldt-Foundation,1971-72
U. Helsinki, Dept. Pharmacy, Assoc. Prof. Pharmacol. Biolog. Standardizaion of Drugs,1972
U. Helsinki and HU Central Hospital, Dept. Clinical Pharmacology, Assistant Professor/Senior Lecturer/Consultant of Clinical Pharmacology, incl. Poison Inform. Cntr.1972-1985
HU Central Hospital, Dept. Internal Medicine, Resident, 1976
U. Helsinki and HU Central Hospital, Dept. Clinical Pharmacology, Acting Professor and Head Physician of Clinical Pharmacology, 1985-1988
U. Turku (Finland), Dept. Pharmacology, Professor & Chairman, 1988-1991
U. Helsinki and HU Central Hospital, Dept. Clinical Pharmacology, Professor & Chairman, and Head Physician, 1992-2011

Supervisor of Doctoral (PhD) Dissertations
Official supervisor, alone or jointly with another supervisor, of 44 Doctoral (PhD) thesis projects at the University of Helsinki or Turku. In addition, a mentor and coauthor in about 20 other PhD projects. Of his former Doctoral students, Professors Klaus Olkkola, Kari Kivistö, Janne Backman, Mikko Niemi and Xiang Xiaoqiang have gained a university professorship.

Reviewer for Professorships

Århus University, Denmark: Professor in Clinical Pharmacology (1992-1993)
Jordan Univ. Science and Technology: Assoc. Professor in Pharmacology (1991)
Odense University, Denmark: Professor in Human Pharmacology (1994, 1995)
University of Helsinki, Finland: Professor in Pharmacology (2001-2002 and 2007)
University of Turku, Finland: Professor in Pharmacology (2010)

Editorial Board Memberships

Clinical Pharmacokinetics, Eur J Clin Pharmacol, Int J Clin Pharmacol Ther, Brit J Clin Pharmacol, Current Diabetes Reviews

Scientific Positions of Trust and Administrative Tasks

Government's Advisory Board on Pharmaceutical Services, Expert Member,1975-2006
Ministry of Social Affairs & Health, National R&D Centre, Clin. Pharmacol. Advisor, 1987-2007
Social Insurance Institute, social medicine and drug committees, Member, 1996-2010
Helsinki Univ. Central Hospital, Drug Advisory Board, Expert Member 1976-87, 1993-2016
Univ. Helsinki/ HU Central Hospital, Ethics Committee, Member 1993-99, Chairman 1997-99
Hospital District of Helsinki & Uusimaa, Coordinating Ethics Comm., Member & Chair, 2000-5

U. Helsinki, Med. Faculty, Clinical Med. Instit., Board member, 1994-8, 03-8, deputy chair 06-8
U. Helsinki, Med. Faculty, Clinical Med. Instit., Chairm. of the Diagnostic-Therap. Dept., 02-11
Finnish Academy of Science & Letters, Member 1998–, Secretary of the Medical group 2005-8
Finnish Clinical Drug Research Graduate School, Founder, and Director 1995-2011

Finnish Pharmacological Society, Board member and Secretary 1977-1985
Finnish Society for Clinical Pharmacology, Board member 1994-2008, Chairman 1994-2000
German Society for Experimental and Clinical Pharmacology and Toxicology, Member
British Pharmacological Society, Member
European Association of Clinical Pharmacology and Therapeutics, Delegate 1996-2002

Awards

The Drug Absorption Foundation Lecturer (Edinburgh) 1993
The Lauri Saxén prize (U. Helsinki) 1997 "for distinguished activities in educating researchers"
The Maud Kuistila prize (Finland) 2003 "to a distinguished instructor of medical researchers"
ISI HighlyCited (pharmacology), in 2005, 2008, 2015, 2016 (ThomsonReuters)
The BCPT Nordic Prize in Basic & Clinical Pharmacology & Toxicology, 2011
FDA Office of Clinical Pharmacology (USA) medal, 2011
Honorary Member of the Finnish Society for Clinical Pharmacology, 2011

Publications

About 515 original articles, and 180 (most in Finnish) reviews or textbook chapters.

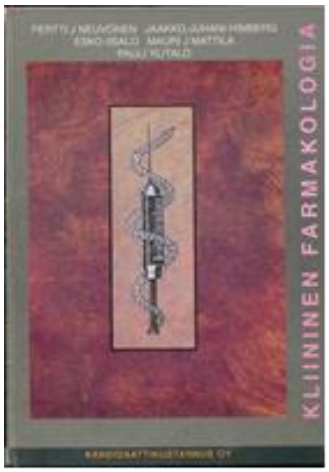
Clin. Pharmacol. Ther.:	92 originals, 1 review
Eur. J. Clin. Pharmacol.:	84 originals
Br. J. Clin. Pharmacol.:	59 originals
Basic & Clin. Pharmacol. & Toxicol.:	36 originals, 3 reviews
Drug Metab. Disposition:	14 originals

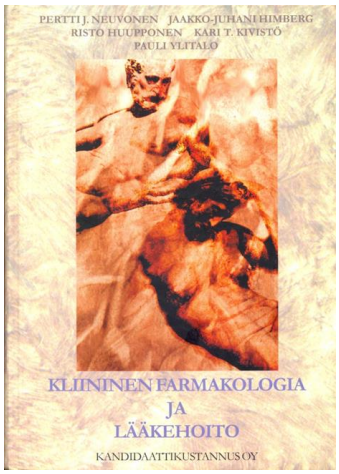
Other journals, e.g., BMJ, Lancet, Diabetologia, Clin. Pharmacokin., Drugs, Pharmacogen. Genomics, Anesthesiology, Anesth. Analgesia, Br. J. Anaesth., Acta Anaesthesiol. Scand., Eur. J. Pharmacol., Br. J. Pharmacol., Int. J. Clin. Pharmacol. Ther. Toxicol., J. Clin. Pharmcol., Drug Safety, Obstetr. Gynecol., Pharmacol. Reviews

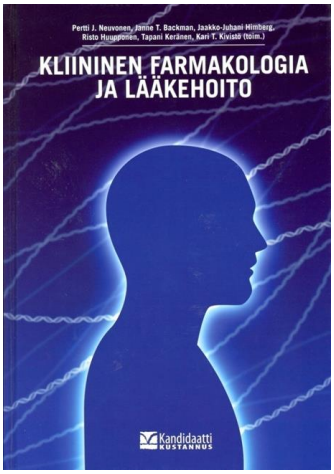
Hirsch Index: 74 (Web of Science, Oct. 2016)
Number of citations: about 21 000.

Textbook in Clinical Pharmacology and Drug Therapy (Kliininen Farmakologia ja Lääkehoito) - Chairman of the Editorial board (and a writer of several chapters) of the Finnish textbook for medical students and clinicians:

1994 (1. ed., 800 pages) 2002 (2. ed., 1067 pages) 2011 (3. ed., 1032 pages)







Research topics

Prof. Neuvonen´s Research topics include several aspects of Clinical Pharmacology, e.g. Clinical Pharmacokinetics, Drug Metabolism and Transport, Drug-Drug Interactions, Food-Drug Interactions, Pharmacogenetics, Effect of Diseases (liver cirrhosis, renal failure, migraine attacks) on Pharmacokinetics, Clinical Toxicology, Acute Intoxications, Adverse Effects, Pharmacoepidemiology, etc.

Detection and exploration of previously unrecognized drug interactions and adverse effects (1970-2016).

Neuvonen published his first drug-drug interaction studies already in the early 1970s, e.g., "Interference of iron with the absorption of tetracyclines in man" (Neuvonen et al., BMJ 1970). This study prompted The Leading Acticle in BMJ, because, at that time, oral tetracyclines and iron preparations were commonly administered to patients with chronic infections. In addition, he also showed that, doxycycline elimination rate was clearly increased in the patients, who used barbiturates (Neuvonen and Penttilä, BMJ 1974) or other inducing antiepileptics, e.g., carbamazepine (Penttilä et al., BMJ 1974), thus increasing the risk of subtherapeutic antibiotic concentrations.

CYP3A-mediated drug interactions. Neuvonen and his co-workers have and published nearly 70 studies on the CYP3A4-mediated drug interactions, since the early 1990s. Their findings have uncovered, e.g., that i**traconazole** (and ketoconazole) can cause **potentially hazardous interactions with, e.g., midazolam, triazolam, buspirone, terfenadine,**

dexamethasone, methylprednisolone, budesonide, lovastatin, simvastatin, atorvastatin, quinidine, digoxin, felodipine, oxycodone and buspirone. The mechanism of these interactions usually is either the inhibition of CYP3A4/5 enzyme, or of P-glycoprotein transporter (as in the case of digoxin), or both**.** The group has characterized also the effects of the doses and routes of administration of victim and perpetrator drugs on the extent of interaction, as well as the duration of the interaction potential.

These findings, which later have been confirmed by many other groups, were in a strong discrepancy with the product information of Sporanox, which in 1992 stated that itraconazole does not inhibit drug metabolism. Today, itraconazole is the recommended probe inhibitor for CYP3A-mediated interaction studies, e.g., in the guidelines of FDA for drug industry. Itraconazole and ketoconazole cause only moderate or minor interactions with prednisolone, pravastatin, zopiclone, zolpidem, morphine, tramadol, ketamine or tzafirlukast. In addition, our group has demonstrated many potential drug interactions caused by fluconazole, voriconazole and miconazole.

After we had found that simvastatin, lovastatin, buspirone, midazolam, and triazolam are sensitive and selective substrates of CYP3A4, we could use these drugs as probes in our further studies, in which the CYP3A-mediated interaction potential of suspected perpetrators were studied in healthy volunteers using standardized conditions and in patients, who used inhibitors or inducers. Thus, we could determine the **interaction potential of many perpetrators such as erythromycin, roxithromycin, azithromycin, chlarithromycin, diltiazem, verapamil, saquinavir, imatinib, grapefruit juice, rifampicin, carbamazepine and St. John Wort, with CYP3A4 substrate drugs.** The results of these studies have been published in more 100 papers between 1993-2016.

Interaction potential of fruit juices. Neuvonen and his co-workers have studied the pharmacokinetic effects of fruit juices since the 1990s. They have found that **grapefruit juice can** markedly, even up to 5-10-fold, **increase the AUC** of many orally ingested drugs (e.g., buspirone, ketamine, oxycodone, simvastatin, lovastatin, atorvastatin, cisapride and ticagrelor (by inhibiting intestinal CYP3A). In contrast to these effects, grapefruit juice, apple juice and orange juice can markedly **decrease the AUC of, e.g., celiprolol** (Lilja et al., 2003) and aliskiren (Tapaninen et al., 2010) by reducing their transporter-mediated absorption. Furthermore, grapefruit juice may **inhibit the metabolic activation** of clopidogrel and prasugrel (Holmberg et al., 2014; 2015).

Statin interactions. Neuvonen and his group discovered in the 1990s, that inhibitors of CYP3A4 can greatly (up to 10-20-fold) increase plasma concentrations of lovastatin, simvastatin and of their active acid forms. The effect on atorvastatin was somewhat smaller. The inhibition of CYP3A4 explained the increased muscle toxicity of these statins caused by, e.g., azole antimycotics, erythromycin derivatives, verapamil and diltiazem, but not the increased toxicity of statins caused by gemfibrozil. We could then show that gemfibrozil increased plasma concentrations of lovastatin acid and of simvastatin acid but not of their parent lactones. This effect of gemfibrozil on statins is mainly caused by an inhibition of the OATP1B1-mediated hepatic uptake, which increases their plasma exposure and muscle toxicity (Neuvonen PJ, Niemi M, Backman JT. Drug interactions with lipid-lowering drugs: Mechanisms and clinical relevance. CPT 2006:80:565-81). The increased muscle toxicity of gemfibrozil-cerivastatin combination has even a more complex mechanism, because its main perpetrator is the glucuronid metabolite of gemfibrozil, which is an inhibitor of both CYP2C8 and OATP1B1.

CYP2C8 in drug metabolism. During the latest 15 years, Prof. Neuvonen, together with his former PhD students and todays Professors Janne Backman and Mikko Niemi, has extensively studied the role of CYP2C8 in the metabolism of drugs, CYP2C8-mediated drug interactions, and inhibitors of CYP2C8. They could identify many generally used drugs, which are mainly metabolized by CYP2C8, or which are potent inhibitors of this enzyme. The interaction potential of these drugs had not been recognized earlier, even though some of them had been in clinical use for decades. **CYP2C8 is responsible for the metabolism and elimination of, e.g., cerivastatin, repaglinide, rosiglitazone, pioglitazone and montelukast. Gemfibrozil and clopidogrel,** mainly via formation of their glucuronid-metabolite**, are potent inhibitors of CYP2C8.** Our observations explain the high risk of, often fatal, muscle toxicity associated with the combined use of cerivastin and gemfibrozil (and of clopidogrel), which led to the withdrawal of cerivastatin from the market in 2001. Similarly, gemfibrozil and clopidogrel can markedly increase the risk of hypoglycaemia when used with repaglinide. These studies on the role of CYP2C8 in drug metabolism and interactions have been published since 2002 in about 40 original papers, and recently reviewed (Backman et al., Pharmacol. Reviews, 2016).

OATP1B1 and other membrane transporters in pharmacokinetics and drug interactions. Together with Professor Niemi and other co-workers, Prof. Neuvonen has studied the significance of OATP1B1, BCRP and some other membrane transporters in the pharmacokinetics and interactions of drugs, e.g., statins. Furthermore, the group has investigated the effect of genetic polymorphisms in membrane transporters on individual differences in pharmacokinetics. In particular, the OATP1B1 has been in focus (Niemi M, Pasanen MK, Neuvonen PJ: Organic anion transporting polypeptide 1B1: a genetically polymorphic transporter of major importance for hepatic drug uptake. Pharmacol. Reviews 2011).

Tizanidine and CYP1A2. Tizanidine had been in clinical use for two decades until Neuvonen´s group discovered that tizanidine nearly exclusively is eliminated by CYP1A2, and that inhibitors of this enzyme drastically increase its plasma concentrations causing potentially life-threatening adverse effects. Fluvoxamine increased the mean AUC of tizanidine more than 30-fold, and ciprofloxacin increased tizanidine AUC more than 10-fold. Tizanidine caused a strong hypotension when ingested with fluvoxamine or ciprofloxacin but not when taken alone (Granfors et al., 2004 x 3).

Acute intoxications can uncover unrecognized properties of drugs. Two cases of **sotalol intoxication**, admitted to the Helsinki University hospital demonstrated for the first time in humans that sotalol prolongs the QT-interval and can cause life-threatening cardiac arrhythmias (Neuvonen et al., 1979). This beta-blocking agent had been in clinical use for nearly 10 years in many countries. In clinical trials, sotalol had been used in huge doses (several grams/day) without any comments on its QT-prolonging or cardiotoxic property. Soon after the publication of these two cases of sotalol intoxication, many similar cases were found in Finland and elsewhere. We could show that also therapeutically used high sotalol doses were associated with considerably prolonged QT-interval and risk of torsade de pointes, thus confirming the earlier unrecognized fact that sotalol is a "different" beta-blocking agent (Neuvonen et al., CPT 1982).

In 1992, five fatal cases of acute serotonin syndrome occurred within 6 months in Finland in subjects who had ingested overdosages of moclobemide-citalopram or moclobemide-clomipramine combinations. Three of these subjects had ingested only a moderate mixed overdose. These cases indicated the substantial risk caused by the combined ingestion of

moclobemide and serotonergic drugs, even after their relatively small overdoses, although moclobemide overdosage alone was known to be relatively harmless.

Activated charcoal as gastric decontaminator in acute drug overdosages.
Neuvonen and his groups have shown in experimental and clinical studies in humans, that activated charcoal, when given in adequate doses and early enough, can substantially reduce gastrointestinal absorption of many drugs, also after ingestion of their high toxic doses. The group has characterized, e.g., the effect of charcoal dose, effect of lag time in its administration, and effect of gastric content on the antidotal effect of orally administered charcoal. In addition, the group has discovered that, given in multiple doses, activated charcoal can accelerate elimination of certain drugs by increasing their excretion into gastrointestinal tract. These, about 40 studies on activated charcoal, performed from the 1980 on, have led to significant changes in treatment of acute intoxications. Today, activated charcoal has replaced, in many cases, Ipecac and gastric lavage as gastrointestinal decontaminant (reviews: Neuvonen,1982; Neuvonen & Olkkola, 1988).

The most cited Publications of Pertti Neuvonen, citation numbers from WoS, Oct. 2016

1. **Neuvonen PJ**, Niemi M, Backman JT: Drug interactions with lipid-lowering drugs: Mechanisms and clinical relevance. Clin Pharmacol Ther 2006:80:565-81. (409 cit.)
2. Niemi M, Backman J, Fromm MF, **Neuvonen PJ**, Kivistö K: Pharmacokinetic interactions with rifampicin: Clinical relevance. Clin Pharmacokinetics 2003;42:819-50. (333 cit.)
3. Olkkola KT, Backman JT, **Neuvonen PJ**: Midazolam should be avoided in patients receiving systemic antimycotics ketoconazole or itraconazole. Clin Pharm Ther 1994:55;481-485. (312 cit.)
4. **Neuvonen PJ**, Kantola T, Kivistö KT: Simvastatin but not pravastatin is very susceptible to interaction with the CYP3A4 inhibitor itraconazole. Clin Pharmacol Ther 1998:63:332-41 (304 cit.)
5. Niemi M, Schaeffeler E, Lang T, Fromm MF, Neuvonen M, Kyrklund C, Backman JT, Kerb R, Schwab M, **Neuvonen PJ**, Eichelbaum M, Kivistö KT: High plasma pravastatin concentrations are associated with single nucleotide polymorphisms and haplotypes of organic anion transporting polypeptide-C (OATP-C, SLCO1B1). Pharmacogenetics 2004:14:429-440. (295 cit.)
6. Pasanen MK, Neuvonen M, **Neuvonen PJ**, Niemi M: SLCO1B1 polymorphism markedly affects the pharmacokinetics of simvastatin acid. Pharmacogenetics & Genomics 2006:16:873-9. (255 cit.)
7. Niemi M, Pasanen MK, **Neuvonen PJ**: Organic anion transporting polypeptide 1B1: a genetically polymorphic transporter of major importance for hepatic drug uptake. Pharmacological Reviews 2011:63:157-181. (251 cit.)
8. Olkkola KT, Aranko K, Luurila H, Hiller A, Saarnivaara L, Himberg J-J, **Neuvonen PJ**: A potentially hazardous interaction between erythromycin and midazolam. Clin Pharmacol Ther 1993:53:298-305. (249 cit.)
9. Niemi M, Backman JT, Kajosaari LI, Leathart JB, Neuvonen M, Daly AK, Eichelbaum M, Kivistö KT, **Neuvonen PJ**: Polymorphic organic anion transporting polypeptide 1B1 is a major determinant of repaglinide pharmacokinetics. Clin Pharmacol Ther 2005:77:468-78. (248 cit.)
10. Backman JT, Kyrklund C, Neuvonen M, **Neuvonen PJ**: Gemfibrozil greatly increases plasma concentrations of cerivastatin. Clin Pharmacol Ther 2002:72:685-91. (231 cit.)

11. Kantola T, Kivistö KT, **Neuvonen PJ**: Erythromycin and verapamil considerably increase serum simvastatin and simvastatin acid concentrations. Clin Pharmacol Ther 1998:64:177-82. (220 cit.)
12. Varhe A, Olkkola KT, **Neuvonen PJ**: Oral triazolam is potentially hazardous to patients receiving systemic antimycotics ketoconazole or itraconazole. Clin Pharmacol Ther 1994:56:601-7. (220 cit.)
13. Pasanen MK, Fredrikson H, **Neuvonen PJ**, Niemi M: Different effects of SLCO1B1 polymorphism on the pharmacokinetics of atorvastatin and rosuvastatin. Clin Pharmacol Ther 2007:82:726-33. (207 cit.)
14. Kantola T, Kivistö KT, **Neuvonen PJ**: Effect of itraconazole on the pharmacokinetics of atorvastatin. Clin Pharmacol Ther 1998:64:58-65. (207 cit.)
15. Lilja JJ, Kivistö KT, **Neuvonen PJ**: Grapefruit-simvastatin interaction: Effect on serum concentrations of simvastatin, simvastatin acid and HMG-CoA reductase inhibitors. Clin Pharmacol Ther 1998:64:477-83. (204 cit.)
16. Backman JT, Kyrklund C, Kivistö KT, Wang J-S, **Neuvonen PJ**: Plasma concentrations of active simvastatin acid are increased by gemfibrozil. Clin Pharmacol Ther 2000:68:122-9. (195 cit.)
17. **Neuvonen PJ**, Jalava M: Itraconazole drastically increases plasma concentrations of lovastatin and lovastatin acid. Clin Pharmacol Ther 1996:60:54-61. (192 cit.)
18. Pentikäinen PJ, **Neuvonen PJ**, Penttilä A: Pharmacokinetics of metformin after intravenous and oral administration to man. Eur J Clin Pharmacol 1979:16:195-202. (188 cit.)
19. Kantola T, Kivistö KT, **Neuvonen PJ**: Grapefruit juice greatly increases serum concentrations of lovastatin and lovastatin acid. Clin Pharmacol Ther 1998:63:397-402. (183 cit.)
20. Keskitalo JE, Zolk O, Fromm MF, Kurkinen KJ, **Neuvonen PJ**, Niemi M: ABCG2 polymorphism markedly affects the pharmacokinetics of atorvastatin and rosuvastatin. Clin Pharmacol Ther 2009:86:197-203. (168 cit.)
21. Backman JT, Olkkola KT, **Neuvonen PJ**: Rifampin drastically reduces plasma concentrations and effects of oral midazolam. Clin Pharmacol Ther 1996:59:7-13. (165 cit.)
22. Niemi M, Backman JT, Neuvonen M, **Neuvonen PJ**: Effects of gemfibrozil, itraconazole, and their combination on the pharmacokinetics and pharmacodynamics of repaglinide: potentially hazardous interaction of repaglinide with gemfibrozil. Diabetologia 2003:46:347-51. (162 cit.)
23. Backman JT, Kivistö KT, Olkkola KT, **Neuvonen PJ**: The area under the plasma concentration-time curve for oral midazolam is 400-fold larger during treatment with itraconazole than with rifampicin. Eur J Clin Pharmacol 1998:54:53-58. (156 cit.)
24. Lilja JJ, Kivistö KT, **Neuvonen PJ**: Grapefruit juice increases serum concentrations of atorvastatin and has no effect on pravastatin. Clin Pharmacol Ther 1999:66:118-27. (154 cit.)
25. **Neuvonen PJ**, Elonen E: Effect of activated charcoal on absorption and elimination of phenobarbitone, carbamazepine and phenylbutazone in man. Eur J Clin Pharmacol 1980:17:51-57. (154 cit.)
26. Olkkola KT, Ahonen J, **Neuvonen PJ**: The effect of the systemic antimycotics, itraconazole and fluconazole, on the pharmacokinetics and pharmacodynamics of intravenous and oral midazolam. Anesth Analg 1996:82:511-516. (150 cit.)
27. Kyrklund C, Backman JT, Kivistö KT, Neuvonen M, Laitila J, **Neuvonen PJ**: Plasma concentrations of active lovastatin acid are markedly increased by gemfibrozil but not by bezafibrate. Clin Pharmacol Ther 2001:69:340-5. (149 cit.)

28. **Neuvonen PJ**, Gothoni G, Hackman R, af Björksten K: Interference of iron with the absorption of tetracyclines in man. Br Med J: 1970:4:532-534. (148 cit.)
29. **Neuvonen PJ**, Pohjola-Sintonen S, Tacke U, Vuori E: Five fatal cases of serotonin syndrome after moclobemide-citalopram or moclobemide-clomipramine overdoses. Lancet 1993:342:1419 (141 cit.)
30. Kajosaari LI, Niemi M, Neuvonen M, Laitila J, **Neuvonen PJ**, Backman JT: Cyclosporine markedly raises the plasma concentrations of repaglinide. Clin Pharmacol Ther 2005:78:388-399. (138 cit.)
31. Niemi M, Pasanen MK, **Neuvonen PJ**: SLCO1B1 polymorphism and sex affect the pharmacokinetics of pravastatin but not fluvastatin. Clin Pharmacol Ther 2006:80:356-66. (137 cit.)
32. Wang J-S, Neuvonen M, Wen X, Backman JT, **Neuvonen PJ**: Gemfibrozil inhibits CYP2C8-mediated cerivastatin metabolism in human liver microsomes. Drug Metabolism and Disposition 2002:30:1352-6. (136 cit.)
33. Backman JT, Olkkola KT, Aranko K, Himberg J-J, **Neuvonen PJ**: Dose of midazolam should be reduced during diltiazem and verapamil treatments. Br J Clin Pharm 1994:37;221-225. (135 cit.)
34. Niemi M, Leathart JB, Neuvonen M, Backman JT, Daly AK, **Neuvonen PJ**: Polymorphism in CYP2C8 is associated with reduced plasma concentrations of repaglinide. Clin Pharmacol Ther 2003:74:380-7. (128 cit.)
35. 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. (128 cit.)
36. Kivistö KT, Kantola T, **Neuvonen PJ**: Different effects of itraconazole on the pharmacokinetics of fluvastatin and lovastatin. Br J Clin Pharmacol 1998:46:49-53. (122 cit.)
37. Vapaatalo H, Onken D, **Neuvonen PJ**, Westermann E: Stereospecificity in central and circulatory effects of phenylisopropyl-adenosine (PIA). Arzneimittel-Forschung (Drug Res) 1975:25:407-410. (121 cit.)
38. **Neuvonen PJ**: Interactions with the absorption of tetracyclines. Drugs 1976:11:45-54. (120 cit.)
39. Malm H, Klaukka T, **Neuvonen PJ**: Risks associated with selective serotonin reuptake inhibitors in pregnancy: a register-based study. Obstetrics and Gynecology 2005:106:1289-96. (117 cit.)
40. **Neuvonen PJ**, Clinical pharmacokinetics of oral activated charcoal in acute intoxications. Clin Pharmacokinet 1982:7:465-489. (114 cit.)
41. Hukkinen SK, Varhe A, Olkkola KT, **Neuvonen PJ**: Effect of grapefruit juice on the bioavailability of triazolam in man. Clin Pharmacol Ther 1995:58:127-131. (112 cit.)
42. Wen X, Wang J-S, Backman JT, Kivistö KT, **Neuvonen PJ**: Gemfibrozil is a potent inhibitor of human cytochrome P450 2C9. Drug Metabolism and Disposition 2001:29:1359-1361. (110 cit.)
43. Wen X, Wang J-S, Backman JT, Laitila J, **Neuvonen PJ**: Trimethoprim and sulfamethoxazole are selective inhibitors of CYP2C8 and CYP2C9, respectively. Drug Metabolism and Disposition 2002:30:631-635. (108 cit.)
44. **Neuvonen PJ**, Backman JT, Niemi M: Pharmacokinetic comparison of the potential over-the-counter statins simvastatin, lovastatin, fluvastatin and atorvastatin. Clinical Pharmacokinetics 2008:47:463-74. (107 cit.)
45. Niemi M, Cascorbi I, Timm R, Kroemer HK, **Neuvonen PJ**, Kivistö KT: Glyburide and glimepiride pharmacokinetics in subjects with different CYP2C9 genotypes. Clin Pharmacol Ther 2002:72:326-32. (102 cit.)

46. Jalava K-M, Partanen J, **Neuvonen PJ**: Itraconazole decreases the renal clearance of digoxin. Therapeutic Drug Monitoring 1997:19:609-13. (102)
47. **Neuvonen PJ**, Vartiainen M, Tokola O: Comparison of activated charcoal and ipecac syrup in prevention of drug absorption. Eur J Clin Pharmacol 1983:24:557-562 (102 cit.)
48. Pasanen MK, **Neuvonen PJ**, Niemi M: Global analysis of genetic variation in SLCO1B1. Pharmacogenomics 2008:9:19-33. (100 cit.)
49. Kajosaari LI, Laitila J, **Neuvonen PJ**, Backman JT: Metabolism of repaglinide by CYP2C8 and CYP3A4 in vitro: effect of fibrates and rifampicin. Basic & Clinical Pharmacol Toxicol 2005:97:249-256. (100 cit.)
50. Niemi M, Backman JT, Granfors M, Laitila J, Neuvonen M, **Neuvonen PJ**: Gemfibrozil considerably increases the plasma concentrations of rosiglitazone. Diabetologia 2003:46:1319-23. (100 cit.)
51. Lilja JJ, Kivistö KT, **Neuvonen PJ**: Duration of effect of grapefruit juice on the pharmacokinetics of the CYP 3A4 substrate simvastatin. Clin Pharmacol Ther 2000:68:384-90. (100 cit.)
52. Pohjola-Sintonen S, Viitasalo M, Toivonen L, **Neuvonen PJ:** Itraconazole prevents terfenadine metabolism and increases risk of torsades de pointes ventricular tachycardia. Eur J Clin Pharmacol 1993:45:191-193. (99 cit.)