

BIBLIOGRAPHY

1. Gaedigk A. Interethnic differences of drug-metabolizing enzymes. *Int J Clin Pharmacol Ther* 2000;**38**:61-8.
2. Wolf CR, Smith G. Pharmacogenetics. *Br Med Bull* 1999;**55**:366-86.
3. Lennard MS. Genetic polymorphism of sparteine/debrisoquine oxidation: A reappraisal. *Pharmacol Toxicol* 1990;**67**:273-83.
4. Nakamura K, Goto F, Ray WA, McAllister CB, Jacqz E. Interethnic differences in genetic polymorphism of debrisoquin and mephenytoin hydroxylation between Japanese and Caucasian populations. *Clin Pharmacol Ther* 1985;**38**:402-8.
5. Sachse C, Brockmoller J, Bauer S, Roots I. Cytochrome P450 2D6 variants in a Caucasian population: allele frequencies and phenotypic consequences. *Am J Hum Genet* 1997;**60**:284-95.
6. Wolf CR, Smith G. Cytochrome P450 *CYP2D6*. *IARC Sci Publ* 1999;**148**:209-29.
7. Masimirembwa CM, Hasler J, Bertilssons L, Johansson I, Ekberg O, Ingelman-Sundberg M. Phenotype and genotype analysis of debrisoquine hydroxylase (*CYP2D6*) in a black Zimbabwean population. Reduced enzyme activity and evaluation of metabolic correlation of *CYP2D6* probe drugs. *Eur J Clin Pharmacol* 1996;**51**:117-22.
8. Lamba V, Lamba JK, Dilawari JB, Kohli KK. Genetic polymorphism of *CYP2D6* in North Indian subjects. *Eur J Clin Pharmacol* 1998;**54**:787-91.

9. Mamidi RNVS, Satyavageeswaram S, Vakkalanka SVS, *et al.* Polymorphism of dextromethorphan oxidation in South Indian subjects. *Clin Pharmacol Ther* 1999;**66**:193-200.
10. Zaingler M, Poor T, Fuhr U. Problems and perspectives of phenotyping for drug-metabolizing enzymes in man. *Int J Clin Pharmacol Ther* 2000;**37**:1-9.
11. Linder MW, Prough RA, Valdes R Jr. Pharmacogenetics: a laboratory tool for optimizing therapeutic efficiency. *Clin Chem* 1997;**43**:254-66.
12. Steiner E, Iselius L, Alvan G, Lindsten J, Sjoqvist F. A family study of genetic and environmental factors determining polymorphic hydroxylation of debrisoquine. *Clin Pharmacol Ther* 1985;**38**:394-401.
13. Garrod AE. The incidence of alcaptonuria: a study in chemical individuality. *Lancet* 1902;**ii**:1616-20.
14. Nebert DW. Pharmacogenetics: 65 candles on the cake. *Pharmacogenetics* 1997;**7**:435-40.
15. Motulsky AG. Drug reactions, enzymes and biochemical genetics. *JAMA* 1957;**165**:835-7.
16. Ingelman-Sundberg M, Oscarson M, McLellan RA. Polymorphic human cytochrome P450 enzymes: an opportunity for individualized drug treatment. *Trends Pharmacol Sci* 1999;**20**:342-9.
17. Lin JH, Lu AYH. Role of pharmacokinetics and metabolism in drug discovery and development. *Pharmacol Rev* 1997;**49**:404-49.

18. Bertilsson L, Dahl ML, Tybring G. Pharmacogenetics of antidepressants: clinical aspects. *Acta Psychiatr Scand* 1997;**96**(suppl 391):14-21.
19. Generation of energy-rich compounds. In: J. Awapara (ed). Introduction to biological chemistry. Published by Prentice-Hall of India Private Limited, New Delhi. 1974; pp147-166 .
20. Nelson DR, Kayonans L, Mamatake T, *et al.* P450 superfamily: update on new sequence, gene mapping, accession numbers and nomenclature. *Pharmacogenetics* 1995;**6**:1-42.
21. Kohler D, Hartter S, Fuchs K, Sieghart W, Hiemke C. CYP2D6 genotype and phenotyping by determination of dextromethorphan and metabolites in serum of healthy controls and of patients under psychotropic medication. *Pharmacogenetics* 1997;**7**:453-61.
22. Shimada T, Yamazaki H, Mimura M, Inui Y, Guengerich FP. Interindividual variation in human liver cytochrome P-450 enzymes involved in oxidation of drugs, carcinogens and toxic chemicals: studies with liver microsomes of 30 Japanese and 30 Caucasians. *J Pharmacol Exp Ther* 1994;**270**:414-23.
23. Wrington SA, Stevens JC. The human hepatic cytochrome P450 involved in drug metabolism. *Crit Rev Toxicol* 1992;**22**:1-21.
24. Gonzalez FJ. Human cytochromes P450: problems and prospects. *Trends Pharmacol Sci* 1992;**13**:346-52.
25. Mahgoub A, Idle JR, Dring LG, Lancaster R, Smith RL. Polymorphic hydroxylation of debisoquine in man. *Lancet* 1977;**2**:584-6.

26. Eichelbaum M, Spannbrucker N, Steincke B, Dangler HJ. Defective N-oxidation of sparteine in man: a new pharmacogenetic defect. *Eur J Clin Pharmacol* 1979;**16**:183-7.
27. Evans DAP, Mahgoub A, Sloan TP, Idle JR, Smith RL. A family and population study of the genetic polymorphism of debrisoquine oxidation in a white British population. *J Med Gen* 1980;**17**:102-5.
28. Kroemer HK, Eichelbaum M "It's the genes, stupid" molecular bases and clinical consequences of genetic cytochrome P450 2D6 polymorphism. *Life Sci* 1995; **56**:2285-98.
29. Woolhouse NM, Eichelbaum M, Oates NS, Idle JR, Smith RL. Dissociation of co-regulatory control of debrisoquine/phenformin and sparteine oxidation in Ghanians. *Clin Pharmacol Ther* 1985;**37**:512-21.
30. Daly AK, Brockmoller J, Broly F, *et al.* Nomenclature for human CYP2D6 alleles. *Pharmacogenetics* 1996;**6**:193-201.
31. Garte S, Crosti F. A nomenclature system for metabolic gene polymorphisms. *IARC Sci Publ* 1999;**148**:5-12.
32. Kimura S, Umeno M, Skoda RC, Mayer UA, Gonzalez FJ. The human debrisoquine 4-hydroxylation (*CYP2D*) locus: sequence and identification of the polymorphic *CYP2D6* gene, a related gene and a pseudogene. *Am J Hum Genet* 1989;**45**:889-904.
33. Gaedigk A, Blum M, Gaedigk R, Eichelbaum M, Mayer UA. Deletion of the entire cytochrome P450 *CYP2D6* gene as a cause of impaired drug

- metabolism in poor metaboliser of the debrisoquine/sparteine polymorphism. *Am J Hum Genet* 1991;**48**:943-50
34. Kagimoto M, Heim M, Kagimoto K, Zeugin T, Mayer UA. Multiple mutations of the human cytochrome P450IID6 gene (CYP2D6) in poor metabolizers of debrisoquine. *J Biol Chem* 1990;**265**:17209-14.
 35. Mayer UA, Skoda RC, Zanger UM. The genetic polymorphism of debrisoquine/sparteine metabolism-molecular mechanisms. *Pharmac Ther* 1990;**46**:297-308.
 36. Gonzalez FJ, Mayer UA. Molecular genetics of the debrisoquine-sparteine polymorphism. *Clin Pharmacol Ther* 1991;**50**:233-8.
 37. Brosen K, Nielsen PN, Brusgaard K, Gram LF, Skjodt K. *CYP2D6* genotype determination in the Danish population. *Eur J Clin Pharmacol* 1994;**47**:221-5.
 38. Funk-Brentano C, Thomas G, Jacqz-Aigrain E, et al. Polymorphism of dextromethorphan metabolism: Relationship between phenotype, genotype, and response to the administration of encainide in humans. *J Pharmacol Exp Ther* 1992;**263**:780-6.
 39. Wang SL, Huang JD, Lai MD, Liu BH, Lai ML. Molecular basis of genetic variation in debrisoquine hydroxylation in Chinese subjects: polymorphism in RFLP and DNA sequence of *CYP2D6*. *Clin Pharmacol Ther* 1993;**53**:410-8.

40. Johansson I, Lundqvist E, Bertilsson L, Dhal ML, Sjoqvist F, Ingelman-Sundberg M. Inherited amplification of an active gene in the cytochrome P450 *CYP2D* locus as a cause of ultrarapid metabolism of debrisoquine. *Proc Natl Acad Sci USA* 1993;**90**:11825-9.
41. May DG. Genetic differences in drug disposition. *J Clin Pharmacol* 1994;**34**:881-97.
42. Smith DA, Jones BC. Speculations on the substrate structure-activity relationship (SSAR) of cytochrome P450 enzymes. *Biochem Pharmacol* 1992;**44**:2089-98.
43. Lennard MS, Tucker GT, Silas JH, Freestone S, Ramsay LE, Woods HF. Differential stereoselective metabolism of metoprolol in extensive and poor debrisoquine metabolisers. *Clin Pharmacol Ther* 1983;**34**:732-7.
44. Chow T, Hiroi T, Imaoka S, Chiba K, Funae Y. Isoform-selective metabolism of mianserin by cytochrom P450 2D. *Drug Metab Dispos* 1999;**27**:1200-4.
45. Weide JVD, Steijns LSW. Cytochrome P450 enzyme system: genetic polymorphisms ad impact on clinical pharmacology. *Ann Clin Biochem* 1999;**36**:722-9.
45. Muralidharan G, Hawes EM, McKay G, Korchinski ED, Midha KK. Quinidine but not quinine inhibits in man the oxidative metabolic routes of

- methoxyphenamine which involve debrisoquine 4-hydroxylase. *Eur J Clin Pharmacol* 1991;**41**:471-4.
47. Brosen K, Skjelbo E. Fluoxetine and norfluoxetine are potent inhibitors of P450IID6-the source of the sparteine/debrisoquine oxidation polymorphism. *Br J Clin Pharmacol* 1991;**32**:136-7.
48. Brynne N, Svanstrom C, Alberg-Wistedt A, Hallen B, Bertilsson L. Fluoxetine inhibits the metabolism of tolterodine-pharmacokinetic implications and proposed clinical relevance. *Br J Clin Pharmacol* 1999;**48**:553-63.
49. Jeppesen U, Gram LF, Vistisen K, Loft S, Poulsen HE, Brosen K. Dose dependent inhibition of *CYP1A2*, *CYP2C19* and *CYP2D6* by citalopram, fluoxetine, fluoxamine and paroxetine. *Eur J Clin Pharmacol* 1996;**51**:73-8.
50. Kroemer HK, Mikus G, Kronbach T, Mayer UA, Eichelbaum M. *In vitro* characterisation of the human cytochrome P450 involved in the polymorphic oxidation of propofenone. *Clin Pharmacol Ther* 1989;**45**:28-33.
51. Adedoyin A, Arns PA, Richards WO, Wilkinson GR, Branch RA. Selective effect of liver disease on the activities of specific metabolizing enzymes: investigation of cytochromes P45 2C19 and 2D6. *Clin Pharmacol Ther* 1998;**64**:8-17.

52. Larrey D, Babany G, Tinel M, *et al.* Effect of liver disease on dextromethorphan oxidation capacity and phenotype: a study in 107 patients. *Br J Clin Pharmacol* 1989;**28**:297-304.
53. Joanee C, Paintaud G, Bresson-Hadni S, *et al.* Is debrisoquine hydroxylation modified during acute viral hepatitis? *Fundam Clin Pharmacol* 1994;**8**:76-9.
54. Eichelbaum M, Mineshita S, Ohnhaus EE, Zekor C. The influence of enzyme induction on polymorphic sparteine oxidation. *Br J Clin Pharmacol* 1986;**22**:49-53.
55. Kallio J, Lindberg R, Huupponen R, Iisalo E. Debrisoquine oxidation in a Finnish population: the effect of oral contraceptives on the metabolic ratio. *Br J Clin Pharmacol* 1988;**26**:791-5.
56. Straka RJ, Hansen SR, Walker PF. Comparison of the prevalence of the poor metabolizer phenotype for CYP2D6 between 203 Hmong subjects and 280 white subjects residing in Minnesota. *Clin Pharmacol Ther* 1995;**58**:29-34.
57. Brosten K. Sparteine oxidation polymorphism in Greenlanders living in Denmark. *Br J Clin Pharmacol* 1986;**22**:415-9.
58. Wanwimolruk S, Patamasucon P, Lee EJD. Evidence for the polymorphic oxidation of debrisoquine in the Thai population. *Br J Clin Pharmacol* 1990;**29**:244-7.
59. Harris RZ, Benet LZ, Schwartz JB. Gender effects in pharmacokinetics and pharmacodynamics. *Drugs* 1995;**50**:222-39.

60. Glimore DA, Gal J, Gerber JG, Nies AS. Age and gender influence the stereoselective pharmacokinetics of propranolol. *J Pharmacol Exp Ther* 1992;**261**:1181-6.
61. Gex-Fabry M, Balant-Gorgia AE, Balant LP, Garrone GL. Clomipramine metabolism: model based analysis of variability factors from drug monitoring data. *Clin Pharmacokinet* 1990;**19**:241-5.
62. Abernethy DR, Greenblatt DJ, Shader RI. Imipramine and desipramine disposition in the elderly. *J Pharmacol Exp Ther* 1985;**232**:183-8.
63. Kashuba ADM, Nafziger AN, Kerns GL, Leeder S, Shirey CS, Hotschall R, *et al.* Quantification of intraindividual variability and the influence of menstrual cycle phase on CYP2D6 activity as measured by dextromethorphan phenotyping. *Pharmacogenetics* 1998;**8**:403-10.
64. Shulman RW, Ozdemir V. Psychotropic medications and cytochrome P450 2D6: pharmacokinetic considerations in the elderly. *Can J Psychiatry* 1997;**42** (Suppl 1):4S-9S.
65. Benitez J, Llerena A, Cobaleda J. Debrisoquine oxidation polymorphism in a Spanish population. . *Clin Pharmacol Ther* 1988;**44**:74-4.
66. He N, Daniel HI, Hajiloo L, Shockley D. Dextromethorphan O-demethylation polymorphism in an African-American population. *Eur J Clin Pharmacol* 1999;**55**:457-9.
67. Llerena AL, Cobaleda J, Martinez C, Benitez J. Inter-ethnic differences in drug metabolism: influence of genetic and environmental factors on

- debrisoquine hydroxylation phenotype. *Eur J Drug Metab Pharmacokinet* 1996;21:129-38.
68. Hogstedt S, Lindberg B, Peng DR, Regardh CG, Rane A. Pregnancy-induced increase in metoprolol metabolism. *Clin Pharmacol Ther* 1985;37:688-92.
69. Wandelius M, Darj E, Frenne G, Rane A. Induction of CYP2D6 in pregnancy. *Clin Pharmacol Ther* 1997;62:400-7.
70. Llerena AL, Puerto AM, Martinez C, *et al.* Debrisoquine oxidation phenotype after ovariectomy. *Eur J Clin Pharmacol Suppl.* 1989;36:A198.
71. Jackson PR, Tucker GT, Woods HF. Testing for bimodality in frequency distributions of data suggesting polymorphisms of drug metabolism-histograms and probit plots. *Br J Clin Pharmac* 1989;28:647-53.
72. Endrenyi L, Patel M. A new, sensitive graphical method for detecting deviations from the normal distribution of drug responses: the NTV plot. *Br J Clin Pharmac* 1991;32:159-66.
73. Schmid B, Bircher J, Preisig R, Kupfer A. Polymorphic dextromethorphan metabolism: cosegregation of oxidative O-demethylation with debrisoquine hydroxylation. *Clin Pharmacol Ther* 1985;38:618-24.
74. Lennard MS, Silas JH, Trevethick J. Defective metabolism of metoprolol in poor hydroxylators of debrisoquine. *Br J Clin Pharmac* 1982;14:301-3.
75. Yue QY, Svensson JO, Alm C, Sjoqvist F, Sawe J. Codeine o-demethylation co-segregates with polymorphic debrisoquine hydroxylation. *Br J Clin Pharmac* 1989;28:639-45.

76. Hou ZY, Pickle LW, Mayer SP, Woosley RL. Salivary analysis for determination of dextromethorphan metabolic phenotype. *Clin Pharmacol Ther* 1991;**49**:410-9.
77. Streetman D, Ellis RE, Nafziger AN. Dose dependency of dextromethorphan for cytochrome P450 2D6 (CYP2D6) phenotyping. *Clin Pharmacol Ther* 1999;**66**:535-41.
78. Hou ZY, Chen CP, Yang WC, *et al.* Determination of dextromethorphan metabolic phenotype by salivary analysis with a reference to genotype in Chinese patients receiving renal hemodialysis. *Clin Pharmacol Ther* 1996;**59**:411-7.
79. Pfaff G, Briegel P, Lamprecht I. Inter-individual variations in the metabolism of dextromethorphan. *Int J Pharmaceut* 1983;**14**:173-89.
80. Marshal PS, Straka RJ, Johnson K. Determination of dextromethorphan and its O-demethylated metabolite from urine. *Ther Drug Monit* 1992;**14**:402-7.
81. Lam YWF, Rodriguez SY. High-performance liquid chromatography determination of dextromethorphan and dextrorphan for oxidation phenotyping by fluorescence and ultraviolet detection. *Ther Drug Monit* 1993;**15**:300-4.
82. Chen ZR, Somogyi AA, Bochner F. Simultaneous determination of dextromethorphan and three metabolites in plasma and urine using high-performance liquid chromatography with application to their disposition in man. *Ther Drug Monit* 1990;**12**:97-104.

83. Bartoletti RA, Belpaire FM, Rosseel MT. High-performance liquid chromatography determination of dextromethorphan and its metabolites in urine using solid phase extraction. *J Pharm Biomed Anal* 1996;**14**:1281-86.
84. Jones DR, Gorski AJC, Hamman MA, Hall SD. Quantification of dextromethorphan and metabolites: a dual phenotypic marker for cytochrome P450 3A4/5 and CYP2D6 activity. *J Chromatogr B* 1996;**678**:105-11.
85. Dixon R, Carbone J, Mohacsi E, Perry C. Dextromethorphan: radioimmuno assay and pharmacokinetic in the dog. *Res Comm Chem Pathol Pharmacol* 1978;**22**:243-55.
86. Freche P, Dragacei S, Petit AM, Siest JP, Galteau MM, Siest G. Development of an ELISA to study the polymorphism of dextromethorphan oxidation in a French population. *Eur J Clin Pharmacol* 1990;**39**:481-5.
87. Frye RF, Matzke GR, Adedoyin A, Porter JA, Branch RA. Validation of the five-drug "Pittsburgh cocktail" approach for assessment of selective regulation of drug-metabolizing enzymes. *Clin Pharmacol Ther* 1997;**62**:365-76.
88. Sachse C, Brockmoller J, Bauer S, Roots I. Cytochrome P450 2D6 variants in a Caucasian population: allele frequencies and phenotypic consequences. *Am J Hum Genet* 1997;**60**:284-95.
89. Daly AK, Steen VM, Fairbrother KS, Idle JR. CYP2D6 Multiallelism. *Methods Enzymol* 1999;**272**:199-210.

90. Heim M, Meyer UA. Genotyping of poor metabolisers of debrisoquine by allele-specific PCR amplification. *Lancet* 1990;**336**:529-32.
91. Aynacioglu AS, Schse C, Bozkurt A et al. Low frequency of defective alleles of cytochrome P450 enzymes 2C19 and 2D6 in the Turkish population. *Clin Pharmacol Ther* 1999;**66**:185-92.
92. Tateishi T, Chida M, Ariyoshi N, Mizorogi Y, Kamataki T, Kobayashi S. Analysis of the *CYP2D6* gene in relation to dextromethorphan O-demethylation capacity in a Japanese population. *Clin Pharmacol Ther* 1999;**65**:570-5.
93. Eichelbaum M, Gross AS. The genetic polymorphism of debrisoquine/sparteine metabolism-clinical aspects. *Pharmac Ther* 1990;**46**:377-94.
94. Balant LP, Balant-Gorgia EA. Cultural differences: implications on drug therapy and global drug development. *Int J Clin Pharmacol Ther* 2000;**38**:47-52.
95. Lou YC. Differences in drug metabolism polymorphism between Orientals and Caucasians. *Drug Metab Rev* 1990;**22**:451-75.
96. Yue QY, Svensson JO, Alm C, Sjoqvist F, Sawe J. Inter-individual and inter-ethnic differences in the dimethylation and glucuronidation of codeine. *Br J Clin Pharmacol* 1989;**28**:629-37.
97. Kalow W. Pharmacogenetics in biological perspective. *Pharmacol Rev* 1997;**49**:369-80

98. Al-Hadidi F, Irshad YM, Rawashdeh NM. Metoprolol α -hydroxylation is a poor probe for debrisoquine oxidation (*CYP2D6*) polymorphism in Jordanians. *Eur J Clin Pharmacol* 1994;**47**:311-4.
99. Johansson I, Oscarson M, Yue QY, Bertilsson L, Sjoqvist F, Ingelman-Sundberg M. Genetic analysis of the Chinese cytochrome P4502D locus: characterization of variant *CYP2D6* genes present in subjects with diminished capacity for debrisoquine hydroxylation. *Mol Pharmacol* 1994;**46**:452-9.
100. Yokota H, Tamura S, Furuya H, et al. Evidence for a new variant allele *CYP2D6J* in a Japanese population associated with lower in vivo rates of sparteine metabolism. *Pharmacogenetics* 1993;**3**:256-63.
101. McLellan RA, Oscarson M, Seidegard J, Evans DA, Ingelman-Sundberg M. Frequent occurrence of *CYP2D6* gene duplication in Saudi Arabians. *Pharmacogenetics* 1997;**7**:187-91.
102. Akillu E, Persson I, Bertilsson L, Johansson I, Rodrigues F, Ingelman-Sundberg M. Frequent contribution of ultra rapid metabolizers of debrisoquine in an Ethiopian population carrying duplicated and multiduplicated functional *CYP2D6* alleles. *J Pharmacol Exp Ther* 1996;**278**:441-6.
103. Idle JR, Smith RL. The debrisoquine hydroxylation gene: a gene of multiple consequences. In *Proceedings of the Second World Conference of Clinical*

Pharmacology and Therapeutics, eds Lemberger L, Reidenberg MM, Washington DC, Am Soc Pharmac Exp Ther 1984;pp148-64.

104. Cavalli-Sforza LL, Piazza A, Menozzi P, Mountain J Reconstruction of human evolution: bringing together genetic, archaeological and linguistic data. *Proc Natl Acad Sci* 1988; **76**:217-225.
105. Lamba JK, Dhiman RK, Kohli KK Genetic polymorphism of the hepatic cytochrome P450C19 in North Indian subjects. *Clin Pharmacol Ther* 1998;**63**:422-427.
106. Weerasurya K, Jayakody RI., Smith AD, Wolf CR, Tucker GT, Lennard MS. Debrisoquine and mephenytoin oxidation in Sinhalese: a population study. *Br J Clin Pharmac* 1994;**38**:466-70.
107. Gutlendre RJ, Britto M, Blouin RA, *et al.* Rapid screening for polymorphisms in dextromethorphan and mephenytoin metabolism. *Br J Clin Pharmac* 1990;**29**:373-80.
108. Relling MV, Cherrie J, Shell MJ, Petros WP, Mayer WH, Evans WE. Lower prevalence of the debrisoquine oxidative poor metaboliser phenotype in American black versus white subjects. *Clin Pharmacol Ther* 1991;**50**:308-13.
109. Otton V, Wu D, Joffe RT, Cheung SW, Sellers EM. Inhibition by fluoxetine of cytochrome P450 2D6 activity. *Clin Pharmacol Ther* 1993;**53**:401-9.
110. Wu D, Otton SV, Spronle BA, *et al.* Inhibition of cytochrome P450 2D6 (CYP2D6) by methadone. *Br J Clin Pharmac* 1993;**35**:30-4.

111. Inaba T, Jurima M, Nakano M, Kalow W. Mephenytoin and sparteine pharmacogenetics in Canadian Caucasians. *Clin Pharmacol Ther* 1984;**36**:670-6.
112. Vinks A, Inaba T, Otton SV, Kalow W. Sparteine metabolism in Canadian Caucasians. *Clin Pharmacol Ther* 1982;**31**:23-29.
113. May GD, Black CM, Olsen NJ, *et al.* Scleroderma is associated with differences in individual routes of drug metabolism: A study with dapsone, debrisoquine and mephenytoin. *Clin Pharmacol Ther* 1990;**48**:286-95.
114. Pert GF, Boutagy J, Shenfield M. Debrisoquine oxidation in an Australian population. *Br J Clin Pharmacol* 1986;**21**:465-71.
115. Veronese M, McLean S. Debrisoquine oxidation polymorphism in a Tasmanian population. *Eur J Clin Pharmacol* 1991;**40**:529-32.
116. Freche P, Dragacci S, Petit AM, Siest JP, Galteau MM, Siest G. Development of an ELISA to study the polymorphism of dextromethorphan oxidation in a French population. *Eur J Clin Pharmacol* 1990;**39**:481-5.
117. Larrey D, Amouyal G, Tinel M *et al.* Polymorphism of dextromethorphan oxidation in a French population. *Br J Clin Pharmacol* 1987;**24**:676-9.
118. Morike K, Platten HP, Mikus G, Klotz U. Variability in the frequency of cytochrome P450-2D6 (*CYP2D6*) deficiency. *Br J Clin Pharmacol* 1998;**46**:87-9

119. Siegmund W, Fengler JD, Franke G, *et al.* N-Acetylation and debrisoquine hydroxylation polymorphisms in patients with Gilbert's syndrome. *Br J Clin Pharmacol* 1991;**32**:467-72.
120. Spina E, Martines C, Caputi AP, *et al.* Debrisoquine oxidation phenotype during neuroleptic monotherapy. *Eur J Clin Pharmacol* 1991;**41**:467-70.
121. Wanwimolruk S, Denton JR, Ferry DG, Beasley M, Broughton JR. Polymorphism of debrisoquine oxidation in New Zealand Caucasian. *Eur J Clin Pharmacol* 1992;**42**:349-50.
122. Augendez JAG, Martinez C, Ledesma MC, Ledona MG, Ladero JM, Benitez J. Genetic basis for differences in debrisoquine polymorphism between Spanish and other white population *Clin Pharmacol Ther* 1994;**55**:412-7.
123. Bertilsson L, Lou QY, Du YL, *et al.* Pronounced differences between native Chinese and Swedish populations in the polymorphic hydroxylations of debrisoquine and s-mephenytoin. *Clin Pharmacol Ther* 1992;**51**:388-97.
124. Steiner E, Bertilsson L, Sawe J, Bertling I, Sjoqvist F. Polymorphic debrisoquine hydroxylation in 757 Swedish subjects. *Clin Pharmacol Ther* 1988;**44**:431-5.
125. Drohse A, Bathum L, Brosen K, Gram LF. Mephenytoin and sparteine oxidation: genetic polymorphism in Denmark. *Br J Clin Pharmacol* 1989;**27**:620-5.

126. Brosen K, Otton SV, Gram LF. Sparteine oxidation polymorphism in Denmark. *Acta Pharmacol Toxicol* 1985;**57**:357-60.
127. Bozkurt A, Basci NE, Isimer A, Sayal A, Kayaalp SO. Polymorphic debrisoquine metabolism in a Turkish population. *Clin Pharmacol Ther* 1994;**55**:399-401.
128. Basci NE, Brosen K, Bozkurt A, Isimer A, Sayal A, Kayaalp SO. S-mephenytoin, sparteine and debrisoquine oxidation: genetic polymorphisms in a Turkish population. *Br J Clin Pharmac* 1994;**38**:463-5.
129. Szorady I, Santa A. Drug hydroxylator phenotype in Hungary. *Eur J Clin Pharmacol* 1987;**32**:325.
130. Estevez F, Giusti M, Parrillo S, Oxandabarat J. Dextromethorphan O-demethylation polymorphism in the Uruguayan population. *Eur J Clin Pharmacol* 1997;**52**:417-8.
131. Arvela P, Kirjarinta M, Kirjarinta M, Karki N, Pelkonen O. Polymorphism of debrisoquine hydroxylation among Finns and Lapps. *Br J Clin Pharmac* 1988;**26**:601-3.
132. Syvalahti EKG, Lindberg R, Kallio J, Vocht MD. Inhibitory effects of neuroleptics on debrisoquine oxidation in man. *Br J Clin Pharmac* 1986;**22**:89-92.

133. Elasen K, Madsen L, Brosen K, Alboge K, Misfeldt S, Gram LF. Sparteine and mephenytoin oxidation: Genetic polymorphism in East and West Greenland. *Clin Pharmacol Ther* 1991;**49**:624-31.
134. Arias TD, Inaba T, Cooke RG, Jorge LF. A preliminary note on the transient polymorphic oxidation of sparteine in the Ngawbe Guaymi Amerindians: A case of genetic divergence with tentative phylogenetic time frame for the pathway. *Clin Pharmacol Ther* 1988;**44**:343-52.
135. Arias TD, Jorge LF. An observation on the ethnic uniqueness of the debrisoquine and sparteine antimodes: a study in the Ngawbe Guaymi Amerindians of Panama. *Br J Clin Pharmac* 1989;**28**:493-4.
136. Arias TD, Jorge LF, Lee D, Barranter R, Inaba T. The oxidative metabolism of sparteine in the Cuna Amerindians of Panama: absence of evidence for deficient metaboliser. *Clin Pharmacol Ther* 1988;**43**:456-65.
137. Aris TD, Jorge LF, Inaba T. No evidence for the presence of poor metaboliser of sparteine in an Amerindian group: the Cunas of Panama. *Br J Clin Pharmac* 1986;**21**:547-8.
138. Iyun AO, Med M, Lennard MS, Tucker GT, Woods HF. Metoprolol and debrisoquine metabolism in Nigerians: Lack of evidence of polymorphic oxidation. *Clin Pharmacol Ther* 1986;**40**:387-94.
139. Bababumi A, Idle JR, Mahgoub A, Mbanefo C, Smith RC. Polymorphic hydroxylation of debrisoquine in Nigerians. *Br J Clin Pharmac* 1980;**9**:112P-3P.

140. Hodjegan, Len MS, Tucker GT. Debrisoquine and metoprolol oxidation in Zambians: a population study. *Br J Clin Pharmacol* 1993;**35**:549P.
141. Bahum L, Skjelbo E, Mutabingwa TK, Madsen H, Horder M, Brosen K. Phenotypes and genotypes for *CYP2D6* and *CYP2C19* in a black Tanzanian population. *Br J Clin Pharmacol* 1999;**48**:395-401.
142. Woolhouse NM, Andoh B, Mahgoub A, Solan TP, Idle JR, Smith RL. Debrisoquine hydroxylation polymorphism among Ghanaians and Caucasians. *Clin Pharmacol Ther* 1979;**26**:584-91.
143. Lane HY, Deng HC, Huang SM, Hu WH, Chang WH, Oliver YPH. Low frequency of dextromethorphan O-demethylation deficiency in a Chinese population. *Clin Pharmacol Ther* 1996;**60**:696-7.
144. Lee EJD, Nam YP, Hee GN. Oxidation phenotyping in Chinese and Malay populations. *Clin Exp Pharmacol Physiol* 1988;**15**:889-91.
145. Sohn DR, Shin SG, Park CW, Kusaka M, Chiba K, Ishizaki T. Metoprolol oxidation polymorphism in a Korean population: comparison with native Japanese and Chinese populations. *Br J Clin Pharmacol* 1991;**32**:504-7.
146. Horai Y, Nakano M, Ishizaki T, Ishizaki K, Zhou HH, Zhou BJ *et al*. Metoprolol and mephenytoin oxidation polymorphism in Far Eastern Oriental subjects: Japanese versus mainland Chinese. *Clin Pharmacol Ther* 1989;**46**:198-207.
147. Lee EJD, Jeyaseelan K. Frequency of human *CYP2D6* mutant alleles in a normal Chinese population. *Br J Clin Pharmacol* 1994;**37**:605-7.

148. Horai Y, Taga J, Ishizaki T, Ishikawa K. Correlations among the metabolic ratios of three test probes (metoprolol, debrisoquine and sparteine) for genetically determined oxidation polymorphism in a Japanese population. *Br J Clin Pharmacol* 1990;**29**:111-5.
149. Horai Y, Ishizaki T, Ishikawa K. Metoprolol oxidation in a Japanese population; evidence for only one poor metaboliser among 262 subjects. *Br J Clin Pharmacol* 1989;**27**:620-5.
150. Ishizaki T, Eichelbaum M, Horai Y, Hashimoto K, Chiba K, Dengler HJ. Evidence of polymorphic oxidation of sparteine in Japanese subjects. *Br J Clin Pharmacol* 1987;**23**:482-5.
151. Wanwimolruk S, Thou MR, Woods DJ. Evidence for the polymorphic oxidation of debrisoquine and proguanil in a Khmer (Cambodian) population. *Br J Clin Pharmacol* 1995;**40**:166-9.
152. Islam SI, Idle JR, Smith RL. The polymorphic 4-hydroxylation of debrisoquine in a Saudi Arabian population. *Xenobiotica* 1980;**10**:819-25.
153. Setiabudy R, Kusaka M, Chiba M, Darmansjah I, Ishizaki T. Dapsone N-acetylation, metoprolol α -hydroxylation and S-mephenytoin 4-hydroxylation polymorphisms in a Indonesian population: A cocktail and extended phenotyping assessment trial. *Clin Pharmacol Ther* 1994;**56**:142-53.
154. Brosen K, Gram LF. Clinical significance of the sparteine/debrisoquine oxidation polymorphism. *Eur J Clin Pharmacol* 1989;**36**:537-47.

155. Spina E, Caputi A. Pharmacogenetic aspects in the metabolism of psychotropic drugs: pharmacokinetic and clinical implications. *Pharmacol Rev* 1994;**29**:121-37.
156. Brosen K, Klysner R, Gram LF, Otton SV, Bech P, Bertilsson L. Steady-state concentrations of imipramine and its metabolites in relation to the sparteine/debrisoquine polymorphism. *Eur J Clin Pharmacol* 1986;**30**:679-84.
157. Spina E, Gitto C, Avenoso A, Campo GM, Caputi AP, Perucca E. Relationship between plasma desipramine levels, *CYP2D6* phenotype and clinical response to desipramine: a prospective study. *Eur J Clin Pharmacol* 1997;**51**:395-84.
158. Dalen P, Dahl ML, Ruiz MLB, Nordin J, ResEng, Bertilsson L. 10-Hydroxylation of nortriptyline in white persons with 0,1,2,3, and 13 functional genes. *Clin Pharmacol Ther* 1998;**63**:444-52.
159. Wolf CR, Smith G, Smith RL. Science, medicine, and the future Pharmacogenetics. *Br Med J* 2000;**320**:987-90.
160. Poulsen L, Arendt-Nielsen L, Brosen K, Sindrup SH. The hypoalgesic effect of tramadol in relation to *CYP2D6*. *Clin Pharmacol Ther* 1996;**60**:336-44.
161. Persson K, Sjostrom S, Sigurdardottir I, Molnar V, Udenaes MH, Rane A. Patient- controlled analgesia (PCA) with codeine for postoperative pain relief in ten extensive metabolisers and one poor metaboliser of dextromethorphan. *Br J Clin Pharmacol* 1995;**39**:182-6.

162. Poulsen L, Brosen K, Arendt-Nielsen L, Gram LF, Elbaek K, Sindrup SH. Codeine and morphine in extensive and poor metabolisers of sparteine: pharmacokinetics, analgesic effect and side effects. *Eur J Clin Pharmacol* 1996;**51**:289-95.
163. Tseng CY, Wang SL, Lai MD, Lai ML, Huang JD. Formation of morphine from codeine in Chinese subjects of different *CYP2D6* genotypes. *Clin Pharmacol Ther* 1996;**60**:177-82.
164. Mikus G, Trausch B, Rodewald C, *et al.* Effect of codeine on gastrointestinal motility in relation to *CYP2D6* phenotype. *Clin Pharmacol Ther* 1997;**61**:459-66.
165. Preskorn SH. Reducing the risk of drug-drug interactions: A goal of rational drug development. *J Clin Psychiatry*, 1996;**57**(suppl 1):3-6.
166. Ozdemir V, Naranjo CA, Hettmann N, Reed K, Seller EM, Kalow W. Paroxetine potentiates the central nervous system side effects of perphenazine: Contribution of cytochrome P4502D6 inhibition in vivo. *Clin Pharmacol Ther* 1997;**62**:334-7.
167. Somer M, Kallio J, Pesonen U, Pyykko K, Huupponen R, Scheinin M. Influence of hydroxychloroquine on the bioavailability of oral metoprolol. *Br J Clin Pharmacol* 2000;**49**:549-54.
168. Naranjo CA, Sproule BA, Knoke DM. Metabolic interactions of central nervous system medications and selective serotonin reuptake inhibitors. *Int Clin Psychopharmacol* 1999;(suppl 2):S35-47.

169. Stanford BJ, Stanford SC. Postoperative delirium indicating an adverse drug interaction involving the selective serotonin reuptake inhibitor, paroxetine? *J Psychopharmacol* 1999;**13**:313-7.
170. Cai WM, Chen B, Zhou Y, Zhang YD. Fluoxetine impairs the *CYP2D6*-mediated metabolism of propafenone enantiomers in healthy Chinese volunteers. *Clin Pharmacol Ther* 1999;**66**:516-21.
171. Kortunay S, Bozkurt A, Bathum I, *et al.* *CYP2D6* polymorphism in Systemic lupus erythematosus patients. *Eur J Clin Pharmacol* 1999;**55**:22-5.
172. Daly AK, Cholerton S, Armstrong M, Idle JR. Genotyping for polymorphisms in xenobiotic metabolism as a predictor of disease susceptibility. *Environ Health Perspect* 1994;**102**:55-61.
173. Kelsey KT, Wensch M, Zuo ZF, Miike R, Wiencke JK. A population-based study of the *CYP2D6* and *GSTT1* polymorphisms and malignant brain tumors. *Pharmacogenetics* 1997;**7**:463-8.
174. Meyer UA, Zanger UM. Molecular mechanisms of genetic polymorphisms of drug metabolism. *Ann Rev Pharmacol Toxicol* 1997;**37**:269-96.
175. Wolf CR, Smith CAD, Forman D. Metabolic polymorphisms in carcinogen metabolising enzymes and cancer susceptibility. *Br Med Bull* 1994;**50**:718-31.

176. Christensen, Gotzsche PC, Brosen K. The sparteine/debrisoquine (CYP2D6) oxidation polymorphism and the risk of lung cancer: a meta-analysis. *Eur J Clin Pharmacol* 1997;**51**:389-93.
177. d' Errico A, Malats N, Vineis P, Boffetta. Review of studies of selected metabolic polymorphisms and cancer. *IARC Sci Publ* 1999;**148**:323-93.
178. Wolf CR, Smith D, Gough CA, *et al.* Relationship between the debrisoquine hydroxylase polymorphism and cancer susceptibility. *Carcinogenesis* 1992;**13**:1035-8.
179. Ladona M, Abildua RE, Ladero JM, *et al.* CYP2D6 genotypes in Spanish women with breast cancer. *Cancer Lett* 1996;**99**:23-8.
180. Jennings M, Sweetland H, Smith CAD, *et al.* Lack of relationship between debrisoquine (CYP2D6) and mephenytoin (CYP2C19) oxidation polymorphisms and susceptibility to cancer. *Breast* 1996;**5**:254-8.
181. Benitez J, Ladero JM, Fernandez-Gundin MJ, *et al.* Polymorphic oxidation of debrisoquine in bladder cancer. *Ann Med* 1990;**22**:157-60.
182. Spurr NK, Gough AC, Chingwundoh FI, Smith D. Polymorphisms in drug metabolising enzymes as modifiers of cancer risk. *Clin Chem* 1995;**41**:1864-9.
183. Brockmoller J, Cascorbi I, Kerb R, Roots I. Combined analysis of inherited polymorphisms in arylamine N-acetyltransferase 2, glutathione S-transferases M1 and T1 microsomal epoxide hydrolase, and cytochrome

- P450 enzymes as modulators of bladder cancer risk. *Cancer Res* 1996;**56**:3915-25.
184. Parret CW, Clayton RN, Pistorello M, *et al.* GSTM1 and CYP2D6 genotype frequencies in patients with pituitary tumors: effects on p53, ras and gsp. *Carcinogenesis* 1995;**16**:1643-5.
185. Barbeau A, Cloutier T, Roy M, Plasses L, Paris S, Poirier J. Ecogenetics of Parkinson's disease: 4-hydroxylation of debrisoquine. *Lancet* 1985;**2**:1213-6.
186. Poirier J, Roy M, Campanella G, Cloutier T, Paris S. Debrisoquine metabolism in Parkinsonian patients treated with antihistamine drugs. *Lancet* 1987;**2**:386.
187. Armstrong M, Daly AK, Cholerton S, Bateman DN, Idle JR. Mutant debrisoquine hydroxylation genes in Parkinson's disease. *Lancet* 1992;**339**:1017-8.
188. Smith CAD, Gough AC, Leigh PN, *et al.* Debrisoquine hydroxylase gene polymorphism and susceptibility to Parkinson's disease. *Lancet* 1992;**339**:1375-7.
189. Chida M, Yokoi T, Kosaka Y *et al.* Genetic polymorphism of *CYP2D6* in the Japanese population. *Pharmacogenetics* 1999;**9**:601-5.
190. Joost O, Taylor CA, Thomas CA, *et al.* Absence of effect of seven functional mutations in the *CYP2D6* gene in Parkinson's disease. *Mov Disord* 1999;**14**:590-5.

191. Edeki T. Clinical importance of genetic polymorphism of drug oxidation. *Mount Sinai J Med* 1996;63:291-300.
192. Chen S, Chou WH, Blouin RA *et al.* The cytochrome P450 2D6 (CYP2D6) enzyme polymorphism: screening costs and influence on clinical outcome in psychiatry. *Clin Pharmacol Ther* 1996;60:522-34.
193. Shu-Qing, Wedlund PJ. Correlation between cytochrome P-450 CYP2D6 (CYP2D6) genotype and phenotype. *Acta Pharmacol Sin* 1999;20:585-8.
194. Birkett DJ, Mackenzie PI, Veronese ME, Miners LO. In vitro approaches can predict human drug metabolism. *Trends Pharmacol Sci* 1993;14:292-4.
195. Engel G, Hofman U, Kroemer HK. Prediction of CYP2D6-mediated polymorphic drug metabolism (sparteine type) based on in vitro investigations. *J Chromatogr B* 1996;678:93-103.
196. Gelboin HV, Krausz KW, Gonzalez FJ, Yang TJ. Inhibitory monoclonal antibodies to human cytochrome P450 enzymes: a new avenue for drug discovery. *Trends Pharmacol Sci* 1999;20:432-8.
197. Gelboin HV, Krausz KW, Shou M, Gonzalez FJ, Yang TJ. A monoclonal antibody inhibitory to human P450 2D6: a paradigm for use in combinatorial determination of individual P450 role in specific drug tissue metabolism. *Pharmacogenetics* 1997;7:469-7.
198. Mathew KM. States and Union Territories. In: *Manorama year book-1998*. Published by Malayala Manorama press, Kottayam, 1998; pp 455-65

199. States and Union Territories. In: India 1998. Published by publication division, Ministry of Information and Broadcasting, Government of India, New Delhi, 1998; pp. 581-668.
200. Emery AEH, Muller RF. Elements of medical genetics. Edinburg, Churchill Livingstone; 1992. pp. 241-64.
201. Singh KS, Bhalla V, Kaul V. The biological variations in Indian populations. Anthropological survey of India. Delhi, Oxford University Press; 1998.
202. Yue QY, Iselius L, Sawe J. Indices and graphical approaches for the detection of interindividual and interethnic variations in codeine metabolism. *Br J Clin Pharmacol* 1997;**44**:239-44.
203. Shu-Qing C, Wedlund PJ. Correlation between cytochrome P450 CYP2D6 (*CYP2D6*) genotype and phenotype. *Acta Pharmacol Sin* 1999;**20**:585-8.
204. Issa AM. Ethical considerations in clinical pharmacogenomics research. *Trends Pharmacol Sci* 2000;**21**:247-9.