|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ID #** | **Authors** | **Year of publication** | **Title** | **Probe Substances** |
| 1 | Funck-Brentano, C. et al. | 1992 | Polymorphism of dextromethorphan metabolism: relationships between phenotype, genotype and response to the administration of encainide in humans | DEX, Encainide |
| 2 | Kolars, J. C. et al. | 1992 | Identification of rifampin-inducible P450IIIA4 (CYP3A4) in human small bowel enterocytes | erythromicin |
| 3 | Sinha et al. | 1994 | Pan-Fried Meat Containing High Levels of Heterocyclic Aromatic Amines but Low Levels of Polycyclic Aromatic Hydrocarbons Induces Cytochrome P4501A2 Activity in Humans | caffeine |
| 4 | Kall, M. A. et al. | 1996 | Effects of dietary broccoli on human in vivo drug metabolizing enzymes: Evaluation of caffeine, oestrone and chlorzoxazone metabolism | caffeine |
| 5 | Le Marchand, L. et al. | 1997 | Lifestyle and nutritional correlates of cytochrome CYP1A2 activity: Inverse associations with plasma lutein and alpha-tocopherol | caffeine |
| 6 | Stillwell, W. G. et al. | 1997 | Urinary excretion of unmetabolized and phase II conjugates of 2-amino- 1-methyl-6-phenylimidazo[4,5-b]pyridine and 2-amino-3,8-dimethylimidazo[4,5- f]quinoxaline in humans: Relationship to cytochrome P4501A2 and N- acetyltransferase activity | caffeine |
| 7 | Adedoyin, A. et al. | 1998 | Chloroquine modulation of specific metabolizing enzymes activities: Investigation with selective five drug cocktail | Caffeine, debrisoquine, dapsone |
| 8 | Burstein, A. H. et al. | 1998 | Cytochrome P450 3A4 activity in premenopausal and postmenopausal women, based on 6-β-hydroxycortisol:cortisol ratios | endogenous marker (cortisol) |
| 9 | McRobie, D. J. Et al. | 1998 | Effects of gestational and overt diabetes on human placental cytochromes P450 and glutathione S-transferase | DEX |
| 10 | Lin, Y. Et al. | 1999 | Differences in the urinary excretion of 6-β-hydroxycortisol/cortisol between Asian and Caucasian women | endogenous marker (cortisol) |
| 11 | Nakajima, M. et al. | 1999 | Genetic polymorphism in the 5'-flanking region of human CYP1A2 gene: Effect on the CYP1A2 inducibility in humans | caffeine |
| 12 | Tennezé, L. et al. | 1999 | Assessment of CYP2D6 and CYP2C19 activity in vivo in humans: A cocktail study with dextromethorphan and chloroguanide alone and in combination | DEX |
| 13 | Wei, X. Et al. | 1999 | Inhibition of human liver cytochrome P-450 1A2 by the class IB antiarrhythmics mexiletine, lidocaine, and tocainide | methoxyresorufin |
| 14 | Becquemont, L. et al. | 2000 | Lymphocyte P-glycoprotein expression and activity before and after rifampicin in man | endogenous marker (cortisol) |
| 15 | Damkier, P. et al. | 2000 | Quinidine as a probe for CYP3A4 activity: Intrasubject variability and lack of correlation with probe-based assays for CYP1A2, CYP2C9, CYP2C19, and CYP2D6 | Caffeine, sparteine, quinidine, endogenous marker (cortisol) |
| 16 | Lampe, J. W. Et al. | 2000 | Brassica vegetables increase and apiaceous vegetables decrease cytochrome P450 1A2 activity in humans: Changes in caffeine metabolite ratios in response to controlled vegetable diets | caffeine |
| 17 | McCune, J. S. et al | 2000 | In vivo and in vitro induction of human cytochrome P4503A4 by dexamethasone | DEX, 14C N-methyl erytromycin |
| 18 | Palovaara, S. et al. | 2000 | Effect of an oral contraceptive preparation containing ethinylestradiol and gestodene on CYP3A4 activity as measured by midazolam 1'-hydroxylation | midazolam |
| 19 | Roby, C. A. et al. | 2000 | St John's Wort: Effect on CYP3A4 activity | endogenous marker (cortisol) |
| 20 | Haas, C. E. et al. | 2001 | Effects of metronidazole on hepatic CYP3A4 activity | 14C N-methyl erytromycin |
| 21 | Han, X. M. et al. | 2001 | Plasma caffeine metabolite ratio (17X/137X) in vivo associated with G-2964A and C734A polymorphisms of human CYP1A2 | caffeine |
| 22 | McCune, J. S. et al. | 2001 | Lack of gender differences and large intrasubject variability in cytochrome P450 activity measured by phenotyping with dextromethorphan | DEX |
| 23 | Nakajima, M. et al. | 2001 | Relationship between interindividual differences in nicotine metabolism and CYP2A6 genetic polymorphism in humans | nicotine |
| 24 | Sofowora, G. G. et al. | 2001 | In vivo inhibition of human CYP1A2 activity by oltipraz | caffeine |
| 25 | Vaziri, S. A. J. Et al. | 2001 | Variation in enzymes of arylamine procarcinogen biotransformation among bladder cancer patients and control subjects | caffeine |
| 26 | Zheng, W. Et al. | 2001 | Epidemiological study of urinary 6β-hydroxycortisol to cortisol ratios and breast cancer risk | endogenous marker (cortisol) |
| 27 | Frye, R. F. et al. | 2002 | Effect of chronic disulfiram administration on the activities of CYP1A2, CYP2C19, CYP2D6, CYP2E1, and N-acetyltransferase in healthy human subjects | Caffeine, debrisoquine |
| 28 | Mouly, S. et al. | 2002 | Hepatic but not intestinal CYP3A4 displays dose-dependent induction by efavirenz in humans | 14C N-methyl erytromycin |
| 29 | Nowak, S. N. et al. | 2002 | Pioglitazone: Effect on CYP3A4 activity | endogenous marker (cortisol) |
| 30 | Kwon, J.T. et al. | 2001 | Nicotine metabolism and CYP2A6 allele frequencies in Koreans | nicotine |
| 31 | Chen, X. P. et al. | 2003 | Isozyme-specific induction of low-dose aspirin on cytochrome P450 in healthy subjects | Caffeine, metoprolol, midazolam |
| 32 | Floyd, M. D. et al. | 2003 | Genotype-phenotype associations for common CYP3A4 and CYP3A5 variants in the basal and induced metabolism of midazolam in European- and African-American men and women | Midazolam, (3N15)-midazolam, 14C N-methyl erytromycin |
| 33 | Markowitz, J. S. et al. | 2003 | Effects of garlic (Allium sativum L.) supplementation on cytochrome P450 2D6 and 3A4 activity in healthy volunteers | DEX, alprazolam |
| 34 | Markowitz, J. S. et al. | 2003 | Multiple-Dose Administration of Ginkgo biloba Did Not Affect Cytochrome P-450 2D6 or 3A4 Activity in Normal Volunteers | DEX, alprazolam |
| 35 | Markowitz, J. S. et al. | 2003 | Multiple doses of saw palmetto (Serenoa repens) did not alter cytochrome P450 2D6 and 3A4 activity in normal volunteers | DEX, alprazolam |
| 36 | Ryu, S. D. et al. | 2003 | Induction of the procarcinogen-activating CYP1A2 by a herbal dietary supplement in rats and humans | caffeine |
| 37 | Veronese, M. L. et al. | 2003 | Exposure-dependent inhibition of intestinal and hepatic CYP3A4 in vivo by grapefruit juice | 14C N-methyl erytromycin, midazolam |
| 38 | DeVane, C. L. et al. | 2004 | Comparative CYP3A4 Inhibitory Effects of Venlafaxine, Fluoxetine, Sertraline, and Nefazodone in Healthy Volunteers | 14C N-methyl erytromycin, alprazolam |
| 39 | Fukami, T. et al. | 2004 | A novel polymorphism of human CYP2A6 gene CTP2A6\*17 has an amino acid substitution (V365M) that decreases enzymatic activity in vitro and in vivo | nicotine |
| 40 | Gurley, B. J. Et al. | 2004 | In vivo assessment of botanical supplementation on human cytochrome P450 phenotypes: Citrus aurantium, Echinacea purpurea, milk thistle, and saw palmetto | Midazolam, caffeine, debrisoquine |
| 41 | Satarug, S. et al. | 2004 | Effects of chronic exposure to low-level cadmium on renal tubular function and CYP2A6-mediated coumarin metabolism in healthy human subjects | coumarin |
| 42 | Wenk, M. et al. | 2004 | Effect of St John's Wort on the activities of CYP1A2, CYP3A4, CYP2D6, N-acetyltransferase 2, and xanthine oxidase in healthy males and females | Caffeine, endogenous marker (cortisol), DEX |
| 43 | El Desoky, E. S. et al. | 2005 | Study of urinary 6β-hydroxycortisol/cortisol ratio in spot urine sample as a biomarker of 3A4 enzyme activity in healthy and epileptic subjects of Egyptian population | endogenous marker (cortisol) |
| 44 | Fukami, T. et al. | 2005 | A novel CYP2A6\*20 allele found in African-American population produces a truncated protein lacking enzymatic activity | nicotine |
| 45 | Gurley, B. J. Et al. | 2005 | In vivo effects of goldenseal, kava kava, black cohosh, and valerian on human cytochrome P450 1A2, 2D6, 2E1, and 3A4/5 phenotypes | Midazolam, caffeine, debrisoquine |
| 46 | Pinto, A. G. et al. | 2005 | Diltiazem inhibits human intestinal cytochrome P450 3A (CYP3A) activity in vivo without altering the expression of intestinal mRNA or protein | midazolam |
| 47 | Pinto, A. G. et al. | 2005 | Inhibition of human intestinal wall metabolism by macrolide antibiotics: Effect of clarithromycin on cytochrome P450 3A4/5 activity and expression | midazolam |
| 48 | Van Heeswijk, R. P. G. et al. | 2005 | Effect of high-dose vitamin C on hepatic cytochrome P450 3A4 activity | 14C N-methyl erytromycin |
| 49 | Chow, H. H. S. et al. | 2006 | Effects of repeated green tea catechin administration on human cytochrome P450 activity | Caffeine, buspirone, DEX |
| 50 | Lambert, G. H. et al. | 2006 | Induced CYP1A2 activity as a phenotypic biomarker in humans highly exposed to certain PCBs/PCDFs | 3-13C-methyl-caffeine |
| 51 | Nakajima, M. et al. | 2006 | Comprehensive evaluation of variability in nicotine metabolism and CYP2A6 polymorphic alleles in four ethnic populations | nicotine |
| 52 | O'Connell, M. B. et al. | 2006 | Effect of conjugated equine estrogens on oxidative metabolism in middle-aged and elderly postmenopausal women | Caffeine, DEX |
| 53 | García-Quetglas, E. et al. | 2007 | Pharmacokinetics of tramadol enantiomers and their respective phase I metabolites in relation to CYP2D6 phenotype | racemic tramadol |
| 54 | Hakooz, N. et al. | 2007 | Effects of dietary broccoli on human in vivo caffeine metabolism: A pilot study on a group of Jordanian volunteers | caffeine |
| 55 | Niewinski, P. et al. | 2007 | Orange juice has no effect on CYPM6-dependent drug-metabolism | sparteine |
| 56 | Somparn, N. et al. | 2007 | Modification of CYP2E1 and CYP3A4 activities in haemoglobin E-beta thalassemia patients | endogenous marker (cortisol) |
| 57 | Tushar, T. et al. | 2007 | Effect of honey on CYP3A4, CYP2D6 and CYP2C19 enzyme activity in healthy human volunteers | endogenous marker (cortisol), DEX |
| 58 | Yao, Y. M. et al. | 2007 | Effect of sinomenine on human cytochrome P450 activity | Midazolam, caffeine, metoprolol |
| 59 | Djordjevic, N. et al. | 2008 | Induction of CYP1A2 by heavy coffee consumption in Serbs and Swedes | caffeine |
| 60 | Karjalainen, M. J. Et al. | 2008 | Celecoxib is a CYP1A2 inhibitor in vitro but not in vivo | Caffeine, tizanidine |
| 61 | Mwenifumbo, J. C. et al. | 2008 | Identification of novel CYP2A6\*1B variants: The CYP2A6\*1B allele is associated with faster in vivo nicotine metabolism | nicotine-d2 and cotinine-d4 |
| 62 | Wang, H. et al. | 2008 | Changes of multiple biotransformation phase I and phase II enzyme activities in human fetal adrenals during fetal development | Coumarin, testosterone |
| 63 | Wink, J. Et al. | 2008 | The effect of a long-term epidural infusion of ropivacaine on CYP2D6 activity | debrisoquine |
| 64 | Al Koudsi, N. et al. | 2009 | A novel CYP2A6 allele (CYP2A6\*35) resulting in an amino-acid substitution (Asn438Tyr) is associated with lower CYP2A6 activity in vivo | nicotine |
| 65 | Chen, Y. | 2009 | Simultaneous action of the flavonoid quercetin on cytochrome p450 (cyp) 1a2, cyp2a6, n-acetyltransferase and xanthine oxidase activity in healthy volunteers | caffeine |
| 66 | Mahavorasirikul, W. et al. | 2009 | CYP2A6 genotypes and coumarin-oxidation phenotypes in a Thai population and their relationship to tobacco smoking | coumarin |
| 67 | Peterson, S. et al. | 2009 | CYP1A2, GSTM1, and GSTT1 polymorphisms and diet effects on CYP1A2 activity in a crossover feeding trial | caffeine |
| 68 | Chen, Y. Et al. | 2010 | Liu Wei Di Huang Wan, a well-known traditional Chinese medicine, induces CYP1A2 while suppressing CYP2A6 and N-acetyltransferase 2 activities in man | caffeine |
| 69 | Chen, Y. Et al. | 2010 | Plant polyphenol curcumin significantly affects CYP1a2 and CYP2a6 activity in healthy, male Chinese volunteers | caffeine |
| 70 | Kjærstad, M. B. et al. | 2010 | Systemic uptake of miconazole during vaginal suppository use and effect on CYP1A2 and CYP3A4 associated enzyme activities in women | Caffeine, quinidine |
| 71 | Li, D. et al. | 2010 | Influence of CYP3A5 and MDR1 Genetic Polymorphisms on Urinary 6β-Hydroxycortisol/ Cortisol Ratio after Grapefruit Juice Intake in Healthy Chinese | endogenous marker (cortisol) |
| 72 | Maezawa, K. Et al. | 2010 | Cytochrome P450 3As Gene Expression and Testosterone 6 beta-Hydroxylase Activity in Human Fetal Membranes and Placenta at Full Term | testosterone |
| 73 | Tao, L. et al. | 2010 | Environmental tobacco smoke in relation to bladder cancer risk - The Shanghai bladder cancer study | caffeine |
| 74 | Chen, Y. Et al. | 2011 | Genistein alters caffeine exposure in healthy female volunteers | caffeine |
| 75 | Dostalek, M. et al. | 2011 | Significantly reduced cytochrome P450 3A4 expression and activity in liver from humans with diabetes mellitus | Midazolam, testosterone |
| 76 | Gebeyehu, E. et al. | 2011 | Sex and CYP3A5 genotype influence total CYP3A activity: High CYP3A activity and a unique distribution of CYP3A5 variant alleles in Ethiopians | Omeprazole, endogenous marker (cholesterol) |
| 77 | Rahmioglu, N. et al. | 2011 | Genetic epidemiology of induced CYP3A4 activity | quinine |
| 78 | Yubero-Lahoz, S. et al. | 2011 | Sex Differences in 3,4-Methylenedioxymethamphetamine (MDMA; Ecstasy)-induced cytochrome P450 2D6 inhibition in humans | DEX |
| 79 | Chiang, H. C. et al. | 2011 | Differential distribution of CYP2A6 and CYP2A13 in the human respiratory tract | none |
| 80 | Yubero-Lahoz, S. et al. | 2012 | Changes in CYP1A2 activity in humans after 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy) administration using caffeine as a probe drug | caffeine |
| 81 | Zadoyan, G. et al. | 2012 | Effect of Ginkgo biloba special extract EGb 761® on human cytochrome P450 activity: A cocktail interaction study in healthy volunteers | Caffeine, DEX, midazolam |
| 82 | Dhuria, S. et al. | 2013 | Time-dependent inhibition and induction of human cytochrome P4503A4/5 by an Oral IAP antagonist, LCL161, in vitro and in vivo in healthy subjects | midazolam |
| 83 | Hassan, R. et al. | 2013 | Genotype-phenotype variability in human CYP3A locus in nepalese people residing in bangladesh | endogenous marker (cortisol) |
| 84 | Perera, V. et al. | 2013 | Diurnal variation in CYP1A2 enzyme activity in South Asians and Europeans | caffeine |
| 85 | Aklillu, E. et al. | 2014 | High CYP2A6 enzyme activity as measured by a caffeine test and unique distribution of CYP2A6 variant alleles in ethiopian population | caffeine |
| 86 | Al-Jenoobi, F. I. et al. | 2014 | Effect of Curcuma longa on CYP2D6- and CYP3A4-mediated metabolism of dextromethorphan in human liver microsomes and healthy human subjects | DEX |
| 87 | Al-Jenoobi, F. I. et al. | 2014 | Modulation of CYP2D6 and CYP3A4 metabolic activities by Ferula asafetida resin | DEX |
| 88 | Al-Jenoobi, F. I. et al. | 2014 | Effect of garden cress seeds powder and its alcoholic extract on the metabolic activity of CYP2D6 and CYP3A4 | DEX |
| 89 | Saruwatari, J. Et al. | 2014 | Effects of seijo-bofu-to, a traditional japanese herbal medicine containing furanocoumarin derivatives, on the drug-metabolizing enzyme activities in healthy male volunteers | endogenous marker (cortisol), DEX, caffeine |
| 90 | Xiao, J. et al. | 2014 | Quercetin Significantly Inhibits the Metabolism of Caffeine, a Substrate of Cytochrome P450 1A2 Unrelated to CYP1A2\*1C (-2964G > A) and\*1F (734C > A) Gene Polymorphisms | caffeine |
| 91 | Bedada, W. Et al. | 2015 | The psychostimulant khat (Catha edulis) inhibits CYP2D6 enzyme activity in humans | DEX |
| 92 | Eichelberger, K. Y. et al. | 2015 | Second-trimester maternal serum paraxanthine, CYP1A2 activity, and the risk of severe preeclampsia | caffeine |
| 93 | Imène, A. et al. | 2015 | Breast cancer association with CYP1A2 activity and gene polymorphisms - A preliminary case-control study in Tunisia | caffeine |
| 94 | Derungs, A. et al. | 2016 | Effects of Cytochrome P450 Inhibition and Induction on the Phenotyping Metrics of the Basel Cocktail: A Randomized Crossover Study | Caffeine, metoprolol, midazolam |
| 95 | Duan, X. Et al. | 2016 | Measurement of human CYP1A2 induction by inhalation exposure to benzo(a)pyrene based on in vivo isotope breath method | 13C-labeled caffeine |
| 96 | Soraoka, H. et al. | 2016 | The Effect of Yokukansan, a Traditional Herbal Preparation Used for the Behavioral and Psychological Symptoms of Dementia, on the Drug-Metabolizing Enzyme Activities in Healthy Male Volunteers | Caffeine, DEX, endogenous marker (cortisol) |
| 97 | Thu, O. K. et al. | 2016 | Effect of commercial Rhodiola rosea on CYP enzyme activity in humans | Caffeine, DEX, midazolam |
| 98 | Begas, E. et al. | 2017 | Effects of peppermint tea consumption on the activities of CYP1A2, CYP2A6, Xanthine Oxidase, N-acetyltranferase-2 and UDP-glucuronosyltransferases-1A1/1A6 in healthy volunteers | caffeine |
| 99 | Tanner, J. A. et al. | 2017 | Predictors of Variation in CYP2A6 mRNA, Protein, and Enzyme Activity in a Human Liver Bank: Influence of Genetic and Nongenetic Factors | Nicotine, coumarin |
| 100 | Tsunoda, S. M. et al. | 1998 | Preliminary evaluation of progestins as inducers of cytochrome P450 3A4 activity in postmenopausal women | 14C N-methyl erytromycin, prednisolone |
| 101 | Kharasch, E. D. et al. | 1999 | Menstrual cycle variability in midazolam pharmacokinetics | midazolam |
| 102 | Wang, Z. et al. | 2001 | The effects of St John's wort (Hypericum perforatum) on human cytochrome P450 activity | Caffeine, midazolam |
| 103 | Abraham, K. et al. | 2002 | Severe 2,3,7,8 -tetrachlorodibenzo:p-dioxin (TCDD) intoxication: Insights into the measurement of hepatic cytochrome P450 1A2 induction | [N-3-methyl-13C]Caffeine |
| 104 | Gashaw, I. et al. | 2003 | Cytochrome p450 3A4 messenger ribonucleic acid induction by rifampin in human peripheral blood mononuclear cells: correlation with alprazolam pharmacokinetics | alprazolam |
| 105 | Veronese, M. L. et al. | 2003 | Effect of mibefradil on CYP3A4 in vivo | 14C N-methyl erytromycin, midazolam |
| 106 | Werner, U. et al. | 2003 | Celecoxib inhibits metabolism of cytochrome P450 2D6 substrate metoprolol in humans | metoprolol |
| 107 | Shadle, C. R. et al. | 2004 | Evaluation of Potential Inductive Effects of Aprepitant on Cytochrome P450 3A4 and 2C9 Activity | midazolam |
| 108 | Aarnoutse, R. E. et al. | 2005 | Effect of low-dose ritonavir (100 mg twice daily) on the activity of cytochrome P450 2D6 in healthy volunteers | Desipramine, DEX |
| 109 | Streit, M. et al. | 2005 | Cytochrome P450 enzyme-mediated drug metabolism at exposure to acute hypoxia (corresponding to an altitude of 4,500 m) | Theophylline, verapamil |
| 110 | Tomalik-Scharte, D. et al. | 2005 | Effect of propiverine on cytochrome P450 enzymes: A cocktail interaction study in healthy volunteers | Midazolam, caffeine |
| 111 | Dadashzadeh, S. et al. | 2006 | The effect of gender on the pharmacokinetics of verapamil and norverapamil in human | verapamil |
| 112 | Kharasch, E. D. et al. | 2007 | Influence of CYP3A5 genotype on the pharmacokinetics and pharmacodynamics of the cytochrome P4503A probes alfentanil and midazolam | Alfentanil, midazolam |
| 113 | Kim, K. A. et al. | 2007 | Effect of polymorphic CYP3A5 genotype on the single-dose simvastatin pharmacokinetics in healthy subjects | simvastatin |
| 114 | Ufer, M. et al. | 2008 | Influence of CYP3A4, CYP3A5, and ABCB1 genotype and expression on budesonide pharmacokinetics: A possible role of intestinal CYP3A4 expression | budesonide |
| 115 | Qiu, F. et al. | 2010 | Effect of danshen extract on the activity of CYP3A4 in healthy volunteers | midazolam |
| 116 | Bello, C. L. et al. | 2012 | The effect of dacomitinib (PF-00299804) on CYP2D6 activity in healthy volunteers who are extensive or intermediate metabolizers | DEX |
| 117 | Zuo, X. C. et al. | 2013 | Effect of CYP3A5\*3 polymorphism on Pharmacokinetic drug interaction between tacrolimus and amlodipine | tacrolimus |
| 118 | Carls, A. et al. | 2014 | Systemic exposure of topical erythromycin in comparison to oral administration and the effect on cytochrome P450 3A4 activity | midazolam |
| 119 | Tao, X. R. et al. | 2015 | CYP3A4∗18B and CYP3A5∗3 polymorphisms contribute to pharmacokinetic variability of cyclosporine among healthy Chinese subjects | cyclosporin |
| 120 | Park et al. | 2017 | Association of CYP2A6 activity with lung cancer incidence in smokers: The multiethnic cohort study | nicotine |
| 121 | Begas et al. | 2018 | Dietary effects of Sideritis scardica “mountain tea” on human in vivo activities of xenobiotic metabolizing enzymes in healthy subjects | caffeine |

**Supplementary Material A**.

Supplementary Material

Supplementary Material A: Open-CYP data base in excel file.

Supplementary Material B. Complete list of the references of the eligible studies extracted and captured in the excel data extraction form.