

# MEDICATIONS AND THE CYTOCHROME P450 HEPATIC ENZYME SYSTEM

SUBSTRATES	<b>1A<sub>2</sub></b>	<b>2C<sub>9/19</sub></b>	<b>2E<sub>1</sub></b>	
SUBSTRATES	<p><b>12.7% of liver content</b></p> <p>acetaminophen (Tylenol)    ropivicaine (Naropin)            caffeine    tacrine (Cognex)            clozapine (Clozaril)    TCA demethylation            cyclobenzaprine (Flexeril)    -amitriptyline (Elavil)            estradiol    -clomipramine (Anafranil)            fluvoxamine (Luvox)    -imipramine (Tofranil)            haloperidol (Haldol)    theophylline (Theo-Dur)            mexiletine (Mexitil)    verapamil (Calan/Isoptin)            naproxen (Anaprox)    R-warfarin (Coumadin)            ondansetron [partly]    Zileuton (Zyflo)              -- (Zofran)            propranolol (Inderal)            phenacetin⇒paracetamol              -(Gripponyl) ⇒ (Tylenol)            riluzone (Rilutek)</p>	<p><b>18.2% of liver content</b></p> <p>carisoprodol (Soma)    (<i>mephenytoin hydroxylase</i>)            celecoxib (Celebrex)    pantoprazole (Pantozol)            citalopram (Celexa)    phenytoin⇒4-OH(Dilantin)            cyclophosphamide (Cytosan)    piroxicam (Feldene)            diazepam (Valium)    primidone (Mysoline) (?)              +desmethyl-diazepam    progesterone              proclofenac (Voltaren)    proguanil [antimalarial]              →cycloguanil            fluoxetine (Prozac)    propranolol (Inderal)            glipizide (Glucotrol)    R-mephobarbital (Mebaral)            hexobarbital (Evipan-Natrium)    R-warfarin ⇒ 8-OH            ibuprofen (Motrin/Advil)    rabeprazole (Aciphex)            indomethacin (Indocin)    rosiglitazone (Avandia)            irbesartan (Avapro)    S-mephenytoin (Epilan)            lansoprazole (Prevacid)    S-naproxen ⇒ Nor-            losartan (Cozaar)    S-warfarin (Coumadin)            mefenamic acid (Ponstel)    sildenafil (Viagra)            moclobemide (Manerix)    sulfamethoxazole (Gantanol)            montelukast (Singulair)    suprofen (Profenal)[ophth]            nelfinavir (Viracept)    tamoxifen (Nolvadex)            nilutamide (Nilandron)    TCA demethylation            omeprazole (Prilosec)    teniposide (Vumon)              <b>2B<sub>6</sub></b>    tolbutamide (Orinase)              bupropion (Wellbutrin)    torsemide (Demadex)              valsartan (Diovan)</p>	<p>acetaminophen            (paracetamol)            aniline            benzene            chlorzoxazone              (Parafon Forte DSC)            enflurane (Ethrane)            Ethyl alcohol            Halothane (Fluothane)            Isoflurane (Forane)            Methoxyflurane (Penthrane)            N,N-dimethylformamide            Sevoflurane (Sevorane)            theophylline⇒8-OH            toxins / carcinogens</p>	
INHIBITORS	<p>amiodarone (Cordarone)    grapefruit juice (?)            cimetidine (Tagamet)    Interferon α2B (Intron A)            ciprofloxacin (Cipro)    methoxsalen (Geroxalen)            cisapride (Propulsid)    mexiletine (Mexitil)            diltiazem (Cardizem)    mibefradil (Posicor)            enoxacin (Penetrex)    norfloxacin (Noroxin)            erythromycin    ritonavir (Norvir) (?)            Ethyl Alcohol [acute]    tacrine (Cognex)            fluoroquinolones    ticlopidine (Ticlid)            fluvoxamine (Luvox)</p>	<p><b>2C<sub>9</sub>:</b></p> <p>amiodarone (Cordarone)            cimetidine (Tagamet)            co-trimoxazole (Bactrim)            disulfiram (Antabuse)            Ethyl Alcohol [acute]            fluconazole (Diflucan)            fluvastatin (Lescol)            isoniazid (INH)            lovastatin (Mevacor)            metronidazole (Flagyl)            norethindrone (Micronor)            omeprazole (Prilosec)            paroxetine (Paxil) (?)            phenylbutazone (Butazolidin)            probenecid (Benemid) (?)            ritonavir (Norvir)            sulfaphenazole            ticlopidine (Ticlid)            trimethoprim (TMP) (?)            zafirlukast (Accolate)</p>	<p><b>2C<sub>9/19</sub>:</b></p> <p>clopidogrel (Plavix)            leflunomide (Arava)            modafinil (Provigil)</p> <p><b>2C<sub>19</sub>:</b></p> <p>cimetidine (Tagamet)            felbamate (Felbatal)            fluvoxamine (Luvox)            fluoxetine (Prozac)            indomethacin (Indocin)            ketoconazole (Nizoral)            lansoprazole (Prevacid)            omeprazole (Prilosec)            paroxetine (Paxil) (?)            probenecid (Benemid) (?)            sertraline (Zoloft) (weak)            ticlopidine (Ticlid)            topiramate (Topamax)</p>	<p>disulfiram (Antabuse)</p>
INDUCERS	<p>beta-naphthoflavone    cigarette smoking [tobacco]            broccoli (?)    Ethyl Alcohol [chronic]            brussel sprouts (?)    insulin            cabbage    methylcholanthrene            carbamazepine (Tegretol)    nevirapine (Viramune)            charbroiled food    omeprazole (Prilosec)</p>	<p>carbamazepine (Tegretol)            cigarette smoking            Ethyl Alcohol [chronic]            nevirapine (Viramune)</p>	<p>norethindrone (Micronor)            prednisone            rifampin (Rifadin)            secobarbital (Seconal)</p>	<p>Ethyl Alcohol [chronic]            isoniazid (INH)</p>
POLY-MORPHISMS	<p><b>CHROMOSOME 15</b></p> <p>2-4% of Caucasians lack            15-25% of Orientals lack</p>	<p><b>CHROMOSOME 10</b></p> <p><b>2C<sub>9</sub>:</b>            5-10% of Caucasians lack            Lower in Asians and            African-Americans</p>	<p><b>POLYMORPHIC</b></p> <p><b>2C<sub>19</sub>:</b>            2-5% Caucasians lack            18-23% of Asians lack            4-19% of African-Americans lack</p>	<p><b>CHROMOSOME 10</b></p>
MORPHISMS	<p>(?) = <i>suspected, but not confirmed</i>  <i>lower case=generic (Capitalized)=(Brand) [brackets]=[information] [combo]=[combination product]</i>  <i>This table is an evolving work in progress.</i>  <i>Information contained within can change based on available literature.</i>  <b>Copyright 1997</b></p>			<p><b>UPDATED 5/2001</b></p>

# MEDICATIONS AND THE CYTOCHROME P450 HEPATIC ENZYME SYSTEM

	<b>2D<sub>6</sub></b>	<b>3A<sub>3/4</sub></b>	
<b>SUBSTRATES</b>	<p><b>1.5% of liver content</b> (<i>debrisoquine hydroxylase</i> or <i>sparteine hydroxylase</i>)</p> <p><b>Antipsychotics</b> clozapine (partially) haloperidol (+reduced) perphenazine (Trilafon) remoxipride (Roxiam) risperidone ⇒ 9-OH (Risperdal) thioridazine (Mellaril) zuclopenthixol (Cisordinol)</p> <p><b>Antidepressants</b> amitriptyline → nortriptyline (Elavil → Pamelor) clomipramine (Anafranil) N-desmethyl-clomipramine fluoxetine (Prozac) norfluoxetine fluvoxamine (Luvox) (?) imipramine → desipramine (Tofranil → Norpramin) maprotiline (Ludiomil) mianserin (Tolvon) minaprine HCl (Cantor) N-desmethyl-citalopram paroxetine (Paxil) sertraline (Zoloft) trazodone (Desyrel) &amp; mCPP metabolite trimipramine (Surmontil) venlafaxine (Effexor)</p> <p><b>Opiates</b> codeine → morphine dextromethorphan morphine</p>	<p><b>28.8% of liver content</b></p> <p>acetaminophen (Tylenol) alfentanil (Alfenta) alprazolam (Xanax) amprenavir (Agenerase) <b>astemizole (Hismanal)</b> atorvastatin (Lipitor) buspirone (BuSpar) carbamazepine (Tegretol) caffeine cerivastatin (Baycol) chlorpheniramine cimetazol (Pletal) <b>cisapride (Propulsid)</b> citalopram (Celexa) clarithromycin (Biaxin) clozapine (Clozaril) cocaine codeine-N-demethylation corticosteroids cyclosporine (Sandimmune) dapstone dexamethasone (Decadron) dextromethorphan (Delsym) diazepam (Valium) diltiazem (Cardizem) erythromycin estrogens efavirenz (Sustiva) felodipine (Plendil) fentanyl (Duragesic) fluvoxamine (Luvox) haloperidol (Haldol) hydrocortisone indinavir (Crixivan) ketoconazole (Nizoral) lansoprazole (Prevacid) lercanidipine (Zanidip) lidocaine (Xylocaine) [partly] losartan (Cozaar) lovastatin (Mevacor)</p>	<p><b>60% of all P450 enzymes</b></p> <p>methadone (Dolophine) midazolam (Versed) mirtazapine (Remeron) modafinil (Provigil) montelukast (Singulair) nefazodone (Serzone) nelfinavir (Viracept) nevirapine (Viramune) nifedipine (Procardia) nisoldipine (Sular) nitrendipine (Bayotensin) O-desmethyl-venlafaxine ondansetron (Zofran) [partly] paclitaxol (taxol) [partly] pioglitazone (Actos) progesterone propafenone (Rythmol) propranolol (Inderal) (?) quinidine (Quinidex) R-warfarin (Coumadin) repaglinide (Prandin) ritonavir (Norvir) salmeterol (Serevent) saquinavir (Invirase) sertraline (Zoloft) sibutramine (Meridia) sildenafil (Viagra) simvastatin (Zocor) sirolimus (Rapamune) tamoxifen (Nolvadex) tacrolimus (Prograf) TCA demethylation-imipramine -amitriptyline / clomipramine <b>terfenadine (Seldane)</b> testosterone theophylline (Theo-Dur) trazodone (Desyrel) triazolam (Xanax) verapamil (Calan) vinblastine (Velban) zaleplon (Sonata) ziprasidone (Geodon)</p>
<b>INHIBITORS</b>	<p>quinidine &gt; fluoxetine (+nor-fluoxetine) &gt; paroxetine &gt; sertraline &gt; fluvoxamine</p> <p>-----</p> <p>amiodarone (Cordarone) chlorpheniramine chlorpromazine (Thorazine) cimetidine (Tagamet) citalopram (Celexa) [weak] clomipramine (Anafranil) cocaine (0.074µM) diltiazem (Cardizem) doxorubicin (Adriamycin) (?) Ethyl Alcohol [acute]</p> <p>fluphenazine (Prolixin) halofantrine (Halfan) haloperidol (Haldol) levomepromazine (Levoprome) methadone (Dolophine) mibefradil (Posicor) moclobemide (Manerix) ranitidine (Zantac) ritonavir (Norvir) TCA's thioridazine (Mellaril) venlafaxine (Effexor) [weak] vincristine (Oncovin) ziprasidone (Geodon) [weak]</p>	<p>amiodarone (Cordarone) cimetidine (Tagamet) ciprofloxacin (Cipro) cisapride (Propulsid) clarithromycin (Biaxin) danazol (Danocrine) diethyl-dithiocarbamate diltiazem (Cardizem) erythromycin (E-Mycin) Ethyl Alcohol [acute] fluconazole (Diflucan) [hi dose] fluoxetine / norfluoxetine (?) fluvoxamine (Luvox) gestodene (Femodene) [combo] grapefruit juice</p>	<p>indinavir (Crixivan) Interferon <i>gamma</i> (Actimmune) itraconazole (Sporanox) ketoconazole (Nizoral) lovastatin (Mevacor) mibefradil (Posicor) mifepristone (Mifegyne) nefazodone (Serzone) nelfinavir (Viracept) omeprazole (Prilosec) quinidine (Quinidex) ritonavir (Norvir) saquinavir (Invirase) sertraline (Zoloft) (?) troleandomycin (Tao)</p>
<b>INDUCERS</b>	<p>barbiturates carbamazepine (Tegretol) cigarette smoking dexamethasone (Decadron) (?)</p> <p>Ethyl Alcohol [chronic] phenytoin (Dilantin) rifampin (Rifadin) (?) valproic acid (Depakene)</p>	<p>barbiturates [incl. Phenobarbital] carbamazepine (Tegretol) cigarette smoking Ethyl Alcohol [chronic] glucocorticoids modafinil (Provigil) nevirapine (Viramune) St. John's Wort (<i>hypericum perforatum</i>)</p>	<p>nevirapine (Viramune) phenylbutazone (Butazolidin) phenytoin (Dilantin) rifabutin (Mycobutin) rifampin (Rifadin) rifapentine (Priftin) rofecoxib (Vioxx) pioglitazone (Rezulin)</p>
<b>POLY-MORPHISMS</b>	<p><b>CHROMOSOME 22</b> <b>POLYMORPHIC</b></p> <p>5-10% of Caucasians have reduced activity 3-10% of Caucasians have twice the enzyme amount 1% of Asians are poor metabolizers Up to 8% of African-Americans are poor metabolizers (?)</p>	<p><b>CHROMOSOME 7</b></p> <div style="border: 2px solid blue; border-radius: 15px; padding: 10px; display: inline-block;"> <p><i>Prepared by Leonard R. Rappa, Pharm.D., BCPP Assistant Professor, Florida A&amp;M University email: rxpsych@yahoo.com</i></p> </div>	