

Table S1. Drugs on top 100 list linked with enzymes and drug transporters involved in metabolism and transportation

| Drugs | Ranking | Phase I enzymes | Phase II enzymes | Drug transporters | References (phase I+II and prodrug) | References (drug transporters) |
|-------------------------------|---------|---|---|-------------------|-------------------------------------|--------------------------------|
| Analgesic | | | | | | |
| Paracetamol | 1 | CYP3A4/5, CYP2E1 | SULT1A1, SULT1A3, SULT1A4, SULT1E1 UGT2B15, UGT1A9, UGT1A6, UGT1A1 | | 1-4 | |
| Codeine* | 7 | CYP3A4/5, CYP2D6 | UGT2B7, UGT2B4 | | 5-7 | |
| Ibuprofen | 12 | CYP2C9, CYP2C8 | UGT1A9, UGT2B7, UGT2B4, UGT1A3 | OAT1, OAT3 | 8,9 | 10 |
| Acetylsalicylic acid* | 18 | CES2 | | | 11,12 | |
| Tramadol* | 21 | CYP3A4/5, CYP2B6, CYP2D6 | | OCT1 | 13,14 | 15 |
| Naproxen | 25 | CYP2C9 (major), CYP2C8, CYP1A2 | UGT1A9, UGT2B7, UGT2B4, UGT1A3 | MCT-1 | 9,16 | 17 |
| Oxycodone | 33 | CYP3A4/5 (major), CYP2D6 | | | 18 | |
| Diclofenac | 35 | CYP3A4/5, CYP2C9 (major), CYP2C19, CYP2C8, CYP2C18, CYP2B6 | UGT2B15, UGT1A9, UGT2B7 (major), UGT1A6 | OAT2 | 19-21 | 22 |
| Gabapentin | 50 | | | OCTN1, LAT1 | | 23 |
| Morphine | 64 | | UGT2B7 | P-gp, OCT1 | 24 | 25,26 |
| Pregabalin | 72 | | | LAT1 | | 27 |
| Ethylmorphine* | 82 | CYP2D6 | | | 28,29 | |
| Dihydrocodeine tartrate | 86 | CYP2D6 | | | 30 | |
| Proton pump Inhibitors | | | | | | |
| Omeprazole* | 4 | CYP3A4/5, CYP2C19 (major) | | P-gp | 31,32 | 33 |

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|--|----|---|--|------------|-------|-------|
| Pantoprazole* | 13 | CYP3A4/5, CYP2C19 (major) | | BCRP | 32,34 | 35 |
| Esomeprazole* | 15 | CYP3A4/5, CYP2C19 (major) | | | 31,32 | |
| Lansoprazole* | 22 | CYP3A4/5, CYP2C19 (major) | | P-gp | 32,36 | 33 |
| Anticoagulants | | | | | | |
| Clopidogrel* | 36 | CYP2C9, CYP2C19, CYP2B6, CYP1A2, CES1 (major) | | P-gp, OAT1 | 37-39 | 40,41 |
| Warfarin | 45 | CYP3A4/5, CYP2C9 (major), CYP2C19, CYP2C8, CYP2C18, CYP1A2 | | OAT2 | 42 | 43 |
| Apixaban | 53 | CYP3A4/5 (major), CYP2C9, CYP2C19, CYP2C8, CYP1A2, CYP2J2 | | P-gp, BCRP | 44 | 45 |
| Rivaroxaban | 67 | CYP3A4/5, CYP2J2 | | P-gp, BCRP | 46 | 47 |
| Antidepressants and antipsychotic | | | | | | |
| Sertralin | 19 | CYP3A4/5, CYP2C9, CYP2C19, CYP2B6, CYP2D6 | | P-gp | 48 | 49 |
| Amitriptylin | 29 | CYP2D6 | | | 50 | |
| Citalopram | 30 | CYP3A4/5 (major), CYP2C19 (major), CYP2D6, MAO-A, MAO- B | | | 51,52 | |
| Mirtazapine | 34 | CYP3A4/5, CYP1A2, CYP2D6 | | | 53 | |
| Escitalopram | 47 | CYP3A4/5, CYP2C19, CYP2D6 | | P-gp | 54 | 55 |

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|-------------------------|----|--|----------------|--|-------|-------|
| Venlafaxine | 48 | CYP3A3, CYP3A4/5, CYP2C9, CYP2C19, CYP2D6 (major) | | | 56,57 | |
| Fluoxetine | 52 | CYP2C9, CYP2C19, CYP2D6 (major) | | | 58 | |
| Quetiapine | 65 | CYP3A4/5 (major), CYP2D6 | | P-gp | 59 | 60 |
| Duloxetine | 85 | CYP1A2, CYP2D6 | | | 61 | |
| Lamotrigine | 88 | | UGT2B7, UGT1A4 | P-gp, BCRP, OCT1 | 62 | 63-65 |
| Antidiabetics | | | | | | |
| Metformin | 9 | | | MATE1, MATE2-K, OCT1, OCT2 (major), SERT, PMAT, THTR-2, CHT | | 66-70 |
| Gliclazide | 69 | CYP2C9 (major), CYP2C19 | | | 71 | |
| Sitagliptin | 89 | CYP3A4/5 (major), CYP2C8 | | P-gp, OAT3, OATP4C1 | 72 | 73 |
| Antibiotics | | | | | | |
| Phenoxymethylpenicillin | 8 | | | | | |
| Amoxicillin | 10 | | | PepT 1, PepT 2 | | 74 |
| Pivmecillinam* | 40 | | | | 75 | |
| Doxycycline | 46 | | | | | |
| Trimethoprim | 55 | CYP3A4/5 (major), CYP2C9 (major), CYP1A2 | | MATE1, MATE2-K | 76 | 77 |
| Flucloxacillin | 61 | CYP3A4/5 (major), CYP3A7, CYP2C9 | | | 78 | |
| Cephalexin | 73 | | | PepT 1 | | 79 |
| Metronidazole* | 75 | CYP2A6 | | | 80,81 | |
| Dicloxacillin | 77 | | | P-gp | | 82 |

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|-----------------------------|-----|---|---------------------------------|---|---------|---------|
| Nitrofurantoin* | 78 | | | BCRP | 83 | 84 |
| Ciprofloxacin | 92 | | | BCRP | | 85 |
| Clindamycin | 100 | CYP3A4/5 (major) | | | 86 | |
| Cardiovascular drugs | | | | | | |
| Amlodipine | 3 | CYP3A4/5 | | | 87 | |
| Ramipril* | 11 | CES1 | | | 88,89 | |
| Losartan | 14 | CYP3A4/5, CYP2C9 | | P-gp | 90 | 91 |
| Metoprolol | 16 | CYP3A4/5, CYP2C9, CYP2B6, CYP2D6 (major) | | | 92,93 | |
| Bisoprolol | 20 | CYP3A4/5 (major), CYP2D6 | | P-gp | 94 | 95 |
| Candesartan cilexetil* | 26 | CYP2C9 | | P-gp, OAT4 | 96,97 | 98,99 |
| Perindopril* | 32 | CES1 | | | 100,101 | |
| Enalapril* | 39 | CES1 | | OATP1B1, OATP1B3, MRP2 | 88,102 | 103 |
| Atenolol | 44 | | | P-gp, MATE1, MATE2-K, OCT1, OCT2 | | 104,105 |
| Irbesartan | 54 | CYP2C9 | | OATP1B1 | 106 | 107 |
| Lisinopril | 57 | | | | | |
| Telmisartan | 59 | | UGT1A3 (major), UGT1A9 | OATP1B3 | 108 | 109 |
| Propranolol | 68 | CYP1A2, CYP2D6 | UGT1A9, UGT2B4, UGT2B7 | P-gp | 110,111 | 112 |
| Lercanidipine | 70 | CYP3A4/5 | | | 113 | |
| Felodipine | 76 | CYP3A4/5 | | | 114 | |
| Valsartan | 80 | CYP2C9 | | OAT1, OAT3, OAT4, OATP1B1, OATP1B3 (major), MRP2 | 115 | 99,116 |

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|-----------------------------------|----|--|------------------------------------|---|-------------|---------|
| Doxazosin | 98 | CYP3A4/5 (major), CYP2C19, CYP2D6 | | | 117 | |
| Cholesterol-lowering drugs | | | | | | |
| Atorvastatin | 2 | CYP3A4/5 | UGT1A1, UGT1A3 | P-gp, OATP1B1, OATP1B3, OATP2B1, MCT | 118,119 | 120,121 |
| Simvastatin* | 5 | CYP3A4/5 | UGT1A1, UGT1A3 | OATP1B1, OATP1B3 | 119,122,123 | 124 |
| Rosuvastatin | 24 | CYP2C9, CYP2C19 | | P-gp, BCRP, OAT3, OATP1A2, OATP1B1, OATP1B3, OATP2B1, MRP2, NTCP | 125 | 126-128 |
| Ezetimibe | 63 | | UGT2B15, UGT2B7, UGT1A3, UGT1A1 | P-gp, MRP2 | 129 | 130,131 |
| Hormones | | | | | | |
| Levothyroxine sodium | 6 | | | | | |
| Ethinylestradiol | 27 | CYP3A4/5 (major), CYP2C9, CYP2C8, CYP2C19, CYP1A2 | SULT1A1, UGT1A1 | | 132-134 | |
| Levonogestrel | 41 | | | | | |
| Estradiol | 42 | CYP3A4/5, CYP1A2, CYP1A1, CYP1B1 | | | 135 | |
| Desogestrel* | 62 | | SULT | | 136,137 | |
| Corticosteroids | | | | | | |
| Prednisolone | 17 | | | | | |
| Dexamethasone | 60 | CYP3A4/5, CES2 | | P-gp | 138 | 139 |
| Diuretics | | | | | | |
| Furosemide | 23 | | UGT1A9 | BCRP, OAT1, OAT3, OATP1B1, | 140 | 141,142 |

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|----------------------|----|--|-------------------------------------|--|---------|---------|
| | | | | OATP1B3, OATP2B1, MRP4 | | |
| Bendroflumethiazide | 31 | | | | | |
| Spironolactone* | 83 | | | | 143 | |
| Hydrochlorothiazide | 96 | | | BCRP, MATE2-K, OAT1 (major), OAT3 (major), OCT2, MRP4 | | 144,145 |
| Sedatives | | | | | | |
| Zopiclone | 28 | CYP3A4/5 (major), CYP2C8 | | | 146 | |
| Diazepam | 43 | CYP3A4/5 (major), CYP2C19, CYP2B6 | | | 147 | |
| Oxazepam | 58 | | UGT2B15, UGT1A9, UGT2B7 | | 148 | |
| Zolpidem | 81 | CYP3A4/5 (major), CYP2C9, CYP2C19, CYP1A2, CYP2D6 | | | 149 | |
| Antihistamine | | | | | | |
| Cetirizine | 37 | | | P-gp, MRP2 | | 150 |
| Desloratadine | 38 | CYP2C8 | UGT2B15, UGT1A3, UGT1A1, UGT2B10 | P-gp | 151,152 | 153 |
| Ranitidine | 71 | CYP2C19, CYP2D6, CYP1A2, FMO3 (major), FMO5 (major) | | P-gp, OCT1, OCT2 | 154 | 155,156 |
| Fexofenadine | 84 | | | P-gp, OATP1B1, OATP1B3 | | 157,158 |
| Loratadine* | 93 | CYP3A4/5 (major), CYP2C9, CYP2C19, CYP2C8, CYP2B6, CYP1A2, CYP1A1, CYP2D6 | | P-gp | 159,160 | |
| Urology | | | | | | |

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|--|----|--|--------|--|-----|---------|
| Tamsulosin | 49 | CYP3A4/5, CYP2D6 | | | 161 | |
| Sildenafil | 66 | CYP3A4/5 (major), CYP2C9 | | P-gp, BCRP | 162 | 163 |
| Antimycotics | | | | | | |
| Fluconazole | 87 | | | P-gp | | 164 |
| Respiratory diseases | | | | | | |
| Montelukast | 91 | CYP3A4/5, CYP2C9, CYP2C19, CYP2C8 | UGT1A3 | | 165 | |
| Other | | | | | | |
| Allopurinol* | 51 | | | BCRP, OAT2 | 166 | 167,168 |
| Alendronic acid | 56 | | | | | |
| Isosorbide mononitrate* | 74 | | | | 169 | |
| Sumatriptan | 79 | MAO-A | | OCT1 | 170 | 171 |
| Metoclopramide | 90 | CYP3A4/5, CYP1A2, CYP2D6 (major) | | P-gp | 172 | 173 |
| Methotrexate | 94 | AO | | P-gp, OATP1B1, OATP1B3, OATP1A2, MRP1, MRP2, MRP3, MRP4 | 174 | 175-179 |
| Finasteride | 95 | CYP3A4/5 | | | 180 | |
| Acetylcysteine* | 97 | | | AE1 | 181 | 182 |
| Methylphenidate | 99 | CES1 | | | 183 | |
| Abbreviation: AE: Anion exchange protein, AO: Aldehyde oxidase, BCRP: Breast Cancer Resistance Protein, CES: Carboxylesterase, CHT: Choline transporter, CYP: Cytochrome P450 enzyme, FMO: Flavin-containing monooxygenase, LAT: L-amino acid transporter, MAO: Monoamine oxidase, MCT: Monocarboxylate Transporter, MRP: Multidrug resistance-associated protein, NTCP: Sodium-taurocholate cotransporting polypeptide, OAT: Organic Anion transporter, OATP: Organic anion transporting polypeptide, OCT: Organic Cation Transporter, OCTN: Organic Cation Transporter Novel, PePT: Peptide transporter, PMAT: Plasma membrane monoamine transporter, P-gp: P-glycoprotein, SERT: Serotonin transporter, SULF: Sulfotransferases, THTR: Thiamin transporter protein, and UGT: Uridine 5'-diphospho-glucuronosyltransferases. | | | | | | |
| *: The drug is a prodrug | | | | | | |

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