

## St. John's Wort Interactions Table

| Drug (Class)<br>Interaction Type                            | Mechanism & Significance  | Management  |
|---|---|---|
| <b>Alprazolam</b><br>(Triazolobenzodiazepines)              | Drug is 3A4 substrate. Herb lowers bioavailability, by inducing 3A4 enzyme production.<br>Interaction proved experimentally,<br>No clinical reports.<br>May be significant for iv midazolam preoperatively.   | Coadministration usually contraindicated,<br>Avoid.   |
| <b>Amitriptyline</b><br>(Tertiary tricyclics)               | Drug is 3A4/P-glycoprotein dual cosubstrate.<br>Herb lowers bioavailability by inducing 3A4 & P-gp.<br>Interaction proved experimentally, no clinical reports.  | Coadministration usually contraindicated,<br>Avoid.   |
| <b>Indinavir/Nevirapine</b><br>(Protease inhibitors/NNRTIs) | Most antiretroviral agents are 3A4/ P-glycoprotein co-substrates.<br>Decreased bioavailability demonstrated.<br>No clinical reports.  | Generally avoid.<br>Coadministration requires specialist supervision and monitoring of drug levels.   |
| Cyclosporine/tacrolimus<br>(Immunosuppressive)              | CsA is cosubstrate of 3A4/P-glycoprotein.<br>Decreased bioavailability demonstrated. Numerous serious reports of graft rejection. Experimental evidence that tacrolimus is also a 3A4 substrate<br>No clinical interactions reports for tacrolimus. | Avoid.  |
| <b>Digoxin</b><br>(Cardiac glycosides)                      | Drug is P-glycoprotein substrate. Possible biphasic response, short term increase, long term decrease in bioavailability,<br>Isolated report of bigeminy (short term).  | If coadministered, ramp/taper the addition/cessation of herb, and monitor drug levels with vigilance during transition.   |
| <b>Etoposide</b><br>(DNA topoisomerase II inhibitors)       | Possible combination pharmacokinetic/ pharmacodynamic interaction, decreased availability (drug is 3A4 substrate) and interference with therapeutic action by hypericin blocking topo II inhibition   | Avoid   |
| <b>Fexofenadine</b><br>(H1 antihistamine)                   | Drug is P-glycoprotein substrate. Decreased bioavailability demonstrated.<br>No clinical reports, minimal significance.   | Unlikely to cause problems,   |
| General Anesthesia  | Potential pharmacokinetic and pharmacodynamic interactions with premeds and/or anesthetic drugs. Reports rare.  | Cessation SJW 1-2 weeks prior to procedure suggested..<br>Pro-op disclosure necessary.  |
| <b>Simvastatin</b><br>(HMG-CoA Reductase Inhibitors)        | Some older statins are cosubstrates of 3A4/P-glycoprotein.<br>Minimal significance, no reports available.   | Consider newer statins if coadministration indicated,   |
| <b>Imatinib</b><br>(Tyrosine kinase inhibitors)             | Gleevec is 3A4 substrate, decreased drug bioavailability demonstrated. Possible compromise to targeted anticancer therapy. No case reports.   | Avoid.  |
| Irinotecan<br>(Camptothecin analogues)                      | Variable pharmacokinetic interaction probable.<br>Significance unknown, CPT-11 responses subject to high inherent variability.  | Avoid.  |
| <b>Omeprazole</b><br>(benzimidazole proton pump inhibitors) | Prilosec is 3A4/2C19 substrate. SJW reduces bioavailability, experimentally demonstrated.<br>No clinical reports, although large size of effect may be clinically significant.  | Avoid, or monitor and increase dose drug.   |
| Combination Oral Contraceptives                             | Hormones are 3A4 substrates. SJW increases breakthrough bleeding, may reduce OC compliance. Contraceptive failure not established despite theoretical risk.   | Avoid, or adopt barrier methods during coadministration.  |
| <b>Paroxetine/Trazodone</b><br>(SSRIs/NSRIs)                | Herb may lead to varying combined pharmacokinetic and pharmacodynamic interactions, at least with some SSRI/NSRI drugs. Mild symptoms of serotonergic excess possible. Several reports of varying reliability. Significance not established.        | Avoid, except with professional monitoring during drug taper.   |
| <b>Phenprocoumon</b><br>(Coumarin anticoagulants)           | Mechanism not established. Possible pharmacokinetic effect, may lead to reduced INR.<br>Significance minimal to moderate.<br>Reliable clinical reports or trials unavailable.   | Unlikely to cause problems. If coadministered, monitor INR once or twice weekly and titrate anticoagulant dosage when starting or stopping SJW therapy, until INR stable. |
| <b>Verapamil</b><br>(Calcium Channel Blockers-[CCBs])       | Verapamil (and all CCBs) are 3A4 substrates, SJW induces intestinal 3A4 and increases drug clearance:<br>No reports; Interaction significance not established   | Monitored co-administration unlikely to cause problems.   |