

# Mechanisms of Serotonin Syndrome and the Drugs Associated with Each

## MECHANISM

## ASSOCIATED DRUGS

Inhibit Serotonin Uptake

**Amphetamines/weight loss drugs:** phentermine  
**Antidepressants:** bupropion, nefazodone, trazodone  
**Antiemetics:** granisetron, ondansetron  
**Antihistamines:** chlorpheniramine  
**Certain opiates:** levomethorphan, levorphanol, meperidine, methadone, pentazocine, pethidine, tapentadol, tramadol  
**Drugs of abuse:** cocaine, MDMA ("Ecstasy")  
**Herbal supplements:** St. John's wort (*Hypericum perforatum*)  
**Over-the-counter cold remedies:** dextromethorphan  
**SNRIs:** desvenlafaxine, duloxetine, venlafaxine  
**SSRIs:** citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline  
**TCAs:** amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine

Inhibit Serotonin Metabolism

**Anxiolytics:** buspirone  
**Herbal supplements:** St. John's wort (*Hypericum perforatum*)  
**MAOIs:** furazolidone, isocarboxazid, linezolid, methylene blue, phenelzine, selegiline, Syrian rue, tranylcypromine  
**Triptans:** almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan

Increase Serotonin Synthesis

**Amphetamines/weight loss drugs:** phentermine  
**Dietary supplements:** L-tryptophan  
**Drugs of abuse:** cocaine

Increase Serotonin Release

**Antidepressants:** mirtazapine  
**Amphetamines/weight loss drugs:** phentermine  
**Certain opiates:** meperidine, oxycodone, tramadol  
**Drugs of abuse:** MDMA ("Ecstasy")  
**Over-the-counter cold remedies:** dextromethorphan  
**Parkinson disease treatment/amino acid:** L-dopa

Activate Serotonin Receptors

**Anxiolytics:** buspirone  
**Antidepressants:** mirtazapine, trazodone  
**Antimigraines:** dihydroergotamine, triptans  
**Certain opiates:** fentanyl, meperidine  
**Drugs of abuse:** LSD  
**Mood stabilizers:** lithium  
**Prokinetic agents:** metoclopramide

Inhibit CYP450 Microsomal Oxidases

**CYP2D6**  
**Inhibitors:** fluoxetine, sertraline  
**Substrates:** dextromethorphan, oxycodone, phentermine, risperidone, tramadol  
**CYP3A4**  
**Inhibitors:** ciprofloxacin, ritonavir  
**Substrates:** methadone, oxycodone, venlafaxine  
**CYP2C19**  
**Inhibitors:** fluconazole  
**Substrates:** citalopram