

# Common antidepressants interact with opioid med to lessen pain relief

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Common antidepressants interact with the opioid pain medication tramadol to make it less effective for pain relief, according to a study from University Hospitals (UH). These findings have important implications for the opioid epidemic, suggesting that some patients suspected of drug-seeking may in fact be under-medicated and just are seeking more effective pain relief. They also could help explain why some people exceed the prescribed dose of tramadol, increasing their risk of addiction.

The study was published in the journal *Pharmacotherapy*.

Researchers reviewed the medication records of 152 [patients](#) at UH Cleveland Medical Center and UH Geauga Medical Center who received scheduled [tramadol](#) for at least 24 hours. All participants in the study were admitted as inpatients or observation status. Those patients who also were taking the antidepressants Prozac (fluoxetine), Paxil (paroxetine) or Wellbutrin (bupropion) required three times more [pain medication](#) per day to control "breakthrough" pain throughout the day, when compared with patients

not taking those antidepressants.

"As we looked at in secondary analysis, it ended up being four times as much over their entire hospital stay," said Derek Frost, a pharmacist at UH and lead author of the study.

Previous studies with healthy volunteers have shown effects on blood levels when combining tramadol with these particular antidepressants. However, this is the first study to document the effects of this interaction in a real-world setting with patients.

"We knew that there was a theoretical problem, but we didn't know what it meant as far as what's happening to pain control for patients," Frost said.

What explains the interaction between tramadol and these antidepressants?

"Tramadol relies on activation of the CYP2D6 enzyme to give you that pain control," Frost said. "This enzyme can be inhibited by medications that are strong CYP2D6 inhibitors, such as fluoxetine, paroxetine and bupropion."

According to Frost, it's likely that millions of Americans may be suffering the ill effects of this drug-to-drug interaction.

"These drugs are super-common," he said. "They're all in the top 200 prescription drugs. In addition, [chronic pain](#) and depression and anxiety go hand in hand. Many chronic pain patients are taking antidepressants, mainly [selective serotonin reuptake inhibitors](#) (SSRIs), which many of these CYP2D6 inhibitors fit into. There are a lot of patients who experience both, unfortunately. The likelihood that somebody on one of these offending agents and tramadol is relatively high."

Fortunately, Frost said, this problem has a relatively easy fix.

"We have a lot of other antidepressants available that are in the same class of medication that don't inhibit this particular enzyme, such as Zoloft (sertraline), (Celexa) citalopram and Lexapro (escitalopram)," he said. "You also have other options for pain control—non-opioid medications such as NSAIDs. If we need to use opioids, a scheduled morphine or a scheduled oxycodone would avoid this interaction."

"For patients who have the combination of chronic [pain](#) and depression or anxiety, keep in mind that this interaction does exist," Frost said. "And for [health care providers](#), if you have a patient approaching you saying this medication isn't working for me, is there an interaction at play?"

**More information:** Derek A. Frost et al. Efficacy of Tramadol for Pain Management in Patients Receiving Strong Cytochrome P450 2D6 Inhibitors, *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* (2019). [DOI: 10.1002/phar.2269](#)

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