**Abuse Resistance of Trypsin-Labile Extended-Release Opioid Prodrugs**

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**Background/Introduction:** We have synthesized extended-release prodrugs oxycodone and hydromorphone. The intent of these opioid prodrugs is to not only provide the expected time course of opioid delivery following oral ingestion, but to preclude extraction of active opioid for parenteral administration using commonly available “kitchen chemistry.” We subjected our opioid prodrugs to Tier 1 (physical manipulations such as crushing and grinding) and Tier 2 (simple extraction procedures using “usable or ingestible” solvents.

**Methods:** We tested our oxycodone and hydromorphone prodrugs for tamper resistance to extraction with 190 proof Everclear, olive oil, vinegar, vodka, baking soda, Coca-Cola® and water. The tests were conducted for 15 minutes and 1 hour, at room temperature and in boiling solutions.

**Results:** Our oxycodone prodrug was subjected to various “kitchen chemistry” conditions and did not release any substantial oxycodone in any of the tests. Our hydromorphone prodrug did not release any measurable oxycodone in any of the tests except for boiling for 1 hour in baking soda, or Coca Cola®, which resulted in release of less than 2% of the hydromorphone.

**Conclusions:** Our extended-release prodrugs of oxycodone and hydromorphone are not amenable to Tier 1 and Tier 2 tampering and abuse using standard crushing and extracting techniques.

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