



Published in final edited form as:

Addiction. 2013 June ; 108(6): 1095–1106. doi:10.1111/add.12114.

A comparison among tapentadol tamper-resistant formulations (TRF) and OxyContin® (non-TRF) in prescription opioid abusers

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Abstract

Aims—To examine whether tamper-resistant formulations (TRFs) of tapentadol hydrochloride ER 50 mg (TAP50) and tapentadol hydrochloride 250 mg (TAP250) could be converted into forms amenable to intranasal (Study 1) or intravenous abuse (Study 2).

Design—Randomized, repeated-measures study designs were employed. A non-TRF of OxyContin® 40 mg (OXY40) served as a positive control. No drug was taken in either study.

Setting—The studies took place in an outpatient setting in New York, NY.

Participants—25 experienced, healthy extended-release oxycodone abusers participated in each study.

Measurements—The primary outcome for Study 1 was percentage of participants who indicated they would snort the tampered tablets, while the primary outcome for Study 2 was percent yield of active drug in solution. Other descriptive variables such as time spent manipulating the tablets were also examined to better characterize tampering behaviors.

Findings—Tampered TRF tablets were less desirable than the tampered OXY40 tablets. Few individuals were willing to snort the TRF particles (TAP50: 24%, TAP250: 16%; OXY40: 100% $p < .001$). There was less drug extracted from the TAP50 tablet than from the OXY40 tablet (3.5% vs. 37.0%, $p = .008$), and no samples from the TAP250 tablets contained analyzable solutions of the drug. It took participants longer to tamper with the TAPs (Study 1: TAP50 vs. OXY40, $p < .01$; TAP250 vs. OXY40, $p < .01$; Study 2: TAP250 vs. OXY40, $p < .05$).

Conclusions—Tapentadol TRF tablets were not well-liked by individuals who regularly tampered with extended-release oxycodone tablets. Employing tamper resistant technology may be a promising approach towards reducing the abuse potential of tapentadol ER.

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Declaration of Interest: Funding for this study was provided by Johnson & Johnson PRD, L.L.C.

Introduction

Prescription opioid medications relieve acute and chronic pain, as well as malignant and non-malignant pain [1–4]. However, these medications are also abused. National survey data reveal that approximately 2 million people aged 12 and older initiated non-medical use of pain relievers in 2010 [5]. An additional 5.1 million people aged 12 years or older were current, non-medical users of pain relievers during the same period of time. Recent data from the Drug Abuse Warning Network (DAWN) reveal that non-medical use of prescription drugs accounted for approximately a quarter of all drug-related ED visits in 2009 [6]. Of those, opioid analgesics accounted for approximately half of the drugs used [6]. While the clinical benefit of these medications is clear, a considerable degree of risk is also associated with their use.

Extended-release opioid formulations were developed for the treatment of pain conditions requiring long-acting, stable levels of medication [7]. When swallowed whole (i.e., taken intact), these formulations have been hypothesized to have a lower abuse potential than immediate release formulations because there is a longer time to peak drug effect [8–9]. Opioid abusers have attempted to circumvent extended-release formulations by crushing the pills for insufflation (“snorting”) or injection (“shooting”) [10] as opioids with rapid rates of onset have been thought to have greater abuse liability [11–13]. Abuse by these routes is also accompanied by increased health risks, such as overdose [14–15], or the transfer of communicable disease [16–20]. Thus, it has been a public health challenge to determine whether it is possible to disrupt opioid tampering while still maintaining the drug delivery necessary to treat pain [21–24].

One development in this area has been the production of abuse deterrent formulations [25]. Mechanisms of available abuse deterrent formulations have been categorized as deterring agents (e.g., naloxone), chemical barriers (e.g., a prodrug), or physical barriers (e.g., hardened tablets) [26]. An example of the physical barrier category are tablets formulated with INTAC™ technology (developed by Grünenthal GmbH; Aachen, Germany). Tablets containing this matrix are difficult to crush, and will gel when combined with small volumes of fluid. This characteristic has been hypothesized to interfere with the ability of individuals to abuse the medication via intranasal and intravenous routes [27–28].

Tapentadol immediate-release (Nucynta®) was developed for moderate to severe acute pain. It is a non-racemic compound that has been characterized as a μ -opioid agonist and a norepinephrine reuptake inhibitor [29–30], with minimal serotonergic effect [31]. It is less potent than morphine, but more potent than tramadol [32]. In a series of preclinical studies in rodents, it was demonstrated that tapentadol was effective in nociceptive, inflammatory, visceral and neuropathic pain models, and was associated with fewer opioid-related side effects (such as emesis and physical dependence) than typical μ -opioid agonists [29].

Tapentadol HCL extended release (Nucynta® ER), was developed for the treatment of chronic pain. Clinically, tapentadol immediate-release and tapentadol extended-release have been compared to oxycodone and have been shown to provide similar levels of pain relief, yet lower levels of gastrointestinal (GI) distress [33–35; see 36 for a review]. Upon consideration of the μ -opioid agonist component along with preliminary data demonstrating that tapentadol generated a similar abuse potential profile of subjective effects as equianalgesic doses of hydromorphone (submitted as part of the NDA application for tapentadol), the DEA and FDA scheduled tapentadol under Schedule II of the Controlled Substances Act. Given this profile, tapentadol ER was formulated with an INTAC™ matrix.

Whether tapentadol ER tablets are able to withstand the tampering attempts of experienced intravenous and intranasal drug abusers is unknown. Thus, the main goal of the present

study was to examine the mechanical stability of the tapentadol 50 mg and 250 mg extended-release tablets (TAP50, TAP250) by determining whether experienced abusers were able to convert the tablets into forms that were amenable to intranasal (Study 1) or intravenous (Study 2) drug administration. An additional aim was to evaluate participants' impressions of the tablets. The original formulation of OxyContin® 40 mg (OXY40) was used as a comparator. OXY40 was chosen because it is a commonly abused prescription opioid, and has been employed as a comparator in a number of other trials with tapentadol [33–35, 37]. No drug was taken, and there was no participant overlap between the studies.

Materials and Methods

Participants

Healthy research volunteers between 21 and 60 years of age who were able to give informed consent were recruited for study participation. Participants had to be currently abusing OxyContin® (or oxycodone) intranasally (Study 1) or intravenously (Study 2) to participate in the studies. Exclusion criteria were current Major Axis I psychopathology other than opioid abuse that could interfere with study participation (e.g., mood disorder with functional impairment, schizophrenia), as well as a history of significant violence, or a significant suicide risk. Participants were recruited through local newspapers and word of mouth.

Design

These were 1-day outpatient studies employing a randomized, repeated-measures design. Participants were provided with OxyContin® 40 mg (OXY40), tapentadol 50 mg ER (TAP50), and tapentadol 250 mg ER (TAP250) tablets in random order. Tablets were referred to as Tablet A, Tablet B, or Tablet C, respectively; the formulation of the tablets was not revealed to participants. Tools that had been specifically requested by the participant for preparing the tablets for abuse were provided. Participants were able to tamper with the tablets for up to an hour to turn them into a form suitable for snorting (Study 1) or shooting (Study 2). These studies were approved by the Institutional Review Board of the New York State Psychiatric Institute (NYSPI) and conducted in 2009.

Procedures

Detailed procedures were described previously [38]. Briefly, after an extensive series of screening interviews and consent procedures, participants were provided with test tablets (OXY40, TAP50, TAP250) in a random sequence under direct supervision of the investigators. Approved tools were provided to them. Investigators recorded the time spent manipulating the tablets with stopwatches. After the tampering procedures were completed, participants responded to scripted questions concerning their impression of the formulations. All participants were paid \$100 before leaving the laboratory.

Upon the completion of each tampering attempt, the senior investigator packaged the tampered samples into storage vials. Batch orders were shipped to Johnson & Johnson Pharmaceutical Research and Development, L.L.C. (Spring House, PA) for particle size analysis (Study 1), or measurement of the volume and drug concentration in the liquid extracts that had been drawn up into syringes (Study 2). With regard to Study 2, all other extracts other than those in syringes (for instance, gelled extracts in vials) were not analyzed because they could not be injected.

Study 1

Outcome Measures

The primary outcome of the Study 1 was percentage of participants who indicated they were willing to snort the prepared tablets. Secondary outcomes were the particle size distribution of the tampered tablets, the actual time spent tampering with the tablets, and the self-reported maximum time participants would be willing to spend on a routine basis preparing the tablets for intranasal abuse. Additional measures collected included the monetary amounts participants were willing to pay for the tablets. Participants were also asked how often they took measures to prevent unwanted particles from ending up in the powder when they prepared OxyContin® for snorting (to estimate the degree of caution that exists in this population regarding insufflation of particles).

Data Analysis

Three contrasts were planned prior to the conduct of the study for primary and secondary outcomes, namely, OXY40 vs. TAP50, OXY40 vs. TAP250, and TAP50 vs. TAP250. Willingness to snort the powder produced was analyzed with the Cochran's Q statistic. Particle size distribution was analyzed with a gravimetric sieve analysis, followed by a high-speed image analysis (HSIA). Samples were passed through a #20 ASTM sieve (850 μ M square perforations). The fraction that was retained on the sieve (i.e., particles > 850 μ M) was considered non-snortable, i.e., not available for snorting. The fraction that passed through the sieve was submitted to the high-speed image analysis with the Sympatec QicPic (Clausthal-Zellerfeld, Germany). These data were summarized with descriptive statistics. Continuous secondary endpoint measures were analyzed with repeated measures ANOVA. Additional data were described with frequency analyses. A degree of variability was expected, thus, it was estimated that a sample size of 25 participants would provide 75% power to detect a 35% difference in a comparison between percentages willing to snort the tampered product. Data analyses were performed with SPSS v. 20.0.0 (IBM), NQuery Advisor v. 4.0 (Statistical Solutions), and SAS v. 9.1.

Results

Twenty-eight participants signed the screening consent form, but 3 did not meet study criteria upon reporting to the laboratory: two for psychiatric reasons, and one who did not meet the inclusion criteria of current OxyContin® use. Table 1 (left panel), presents the demographic characteristics of the 25 participants who completed the study. Fifty-two percent reported using OxyContin® to treat pain before recreational opioid use was initiated. Table 2 (left panel) presents the tools and solvents used by participants to prepare the tablets for insufflation.

Primary Outcome Measure

All participants (100%) were willing to snort the powder produced from the OXY40 tablet, compared to 24% who were willing to snort the powder produced from the TAP50 tablet, and 16% who were willing to snort the TAP250 tablet. The differences between OXY40 and both doses of TAP were statistically significant (Cochran's $Q_{(2)} = 38.38$; $p < .001$; OXY40 vs. TAP50, $p < .01$; OXY40 vs. TAP250, $p < .01$). There were no statistically significant differences between the percentages of participants who were willing to snort TAP50 or TAP250.

Table 3 summarizes verbatim explanations participants provided when asked why they would (or would not) snort the tampered product. Figure 1, **top panel** depicts representative photographic samples from OXY40, TAP50 and TAP250. OXY40 tablets could be crushed

into a fine powder whereas both TAP formulations could only be cut into large, jagged particles.

Secondary Outcome Measures

Particle size—Particle size data are presented in Table 4. Lower percentages of the initial, intact tablet by weight were recovered as tampering products from the OXY40 tablets than from TAP50 or TAP250. This was likely due to the fine powder produced from the OXY40 during the crushing process which stuck to the work surface or potentially blew away during the product transfer. The OXY40 powder that filtered through the #20 ASTM sieve mesh represented an average of 79.2% of the weight of the recovered OXY40, whereas 20.8% was left on the mesh screen. The average number of particles (smaller than 850 μm) available for a dose of OXY40 was 41,595. HSIA analysis revealed that the particles were, in general, uniformly shaped and predominantly spherical. Figure 2, **top panel**, depicts shapes of the OXY40 tablets from the HSIA.

In contrast to the results for OXY40, most of the TAP50 and TAP250 particles did not pass through the #20 ASTM sieve mesh because they were too large. The amounts that passed through represented 2.1% and 1.3% of the weight of the TAP50 and TAP250 tablets, respectively. HSIA analysis revealed that these particles were large, jagged, and irregular Figure 2, **lower panel**. Thus, particle size analyses revealed that both TAP formulations produced fewer particles that accounted for less of the tablet weight than the OXY40 formulation (all p s <.001), while there were no differences between the two TAP formulations.

Time Preparing Tablets—Table 5 demonstrates that participants spent more time preparing the TAP50 and TAP250 tablets than the OXY40 tablet. Participants reported that they were willing to spend more time preparing the TAP50 and the TAP250 tablets for use than the OXY40 tablets.

Relative Perceived Monetary Value and Removing Unwanted Particles—Table 6 presents *verbatim* responses to the question of whether participants would pay “Less,” “More,” or “The Same” for a tablet that took substantially more time and effort to prepare for snorting than for a tablet with the same amount of drug that was easier to prepare. The majority of participants would pay “Less,” whereas the remainder would pay “The Same” for such a tablet. It was notable that none were willing to pay “More” than for a tablet that was easier to prepare. Table 7 reveals that most participants (68%) “Always” or “Usually” took measures to prevent unwanted particles from ending up in the powder when preparing an OXY40 tablet for abuse.

Study 2

Outcome Measures

The primary endpoint was the percent yield of active drug in solution that participants were able to obtain from the OXY40, TAP50 and TAP250 tablets. Secondary outcomes were the self-reported willingness to inject the tampered product, the actual time spent tampering with the tablets, and the self-reported maximum time participants would be willing to spend on a routine basis preparing the tablets for abuse. Additional data collected were similar to Study 1.

Data Analysis

As in Study 1, three contrasts were planned prior to the conduct of the study for primary and secondary outcomes, namely, OXY40 vs. TAP50, OXY40 vs. TAP250, and TAP50 vs.

TAP250. To determine the percent yield of active drug that was recovered, the mg of active drug recovered was divided by the mg of active drug in the tablet label claim. Percent yield was summarized with descriptive statistics, and compared with the non-parametric Wilcoxon signed rank test to reflect the non-normal distribution of the data. It was estimated that a sample size of 25 participants would provide approximately 80% power to detect a 15% difference in yield between the formulations, assuming a standard deviation of 25% yield. Other measures were analyzed and reported as in Study 1.

Results

Table 1 (right panel) presents the demographic characteristics of the 25 participants who completed the study. There were no screen failures. Twenty-eight percent reported using OxyContin® to treat pain before recreational opioid use was initiated. Table 2 (right panel) presents the tools and solvents used by participants to prepare the tablets for intravenous use. Hammers were used to crush the tablets, spoons were used to hold the tablet fragments, lighters were used to heat a solution of tablet fragments and solvent, while cotton was used as a filter through which the extract was drawn up into the syringe.

Primary Outcome Measure

Amount of active drug in solution—The average percent yield of OXY40 was 37.02% ($\pm 16.67\%$), representing a mean of 14.8 mg of active drug (± 6.7 mg) per 40 mg tablet. The average percent yield of TAP50 was 3.52% ($\pm 2.77\%$), representing a mean of 1.76 mg (± 1.4 mg) of active drug per 50 mg tablet. Both the mean percentage and average amount (in mg) of drug recovered were greater in the OXY40 dataset (Wilcoxon signed-rank test for both comparisons: $Z=2.67$, $p=.008$). No active drug was extracted as a liquid into a syringe from the TAP250 tablets by any of the participants. Figure 1, **bottom panel** depicts the solutions produced from each tablet. As can be seen, approximately 25ccs of clear solution was drawn up from the OXY40 tablet, whereas both TAP tablets primarily produced chunky, partially-gelled solutions.

Secondary Outcome Measures

Time Preparing Tablets—Table 8 presents the analyses of time spent preparing tablets. Planned contrasts revealed that participants spent longer preparing TAP250 than OXY40. There were no differences among the maximum amounts of time that participants would be willing to spend preparing tablets for intravenous use.

Willingness to Inject—Table 9 presents the data describing percentages of participants who would inject the solutions produced from the tampering attempts. All participants were willing to inject the OXY40, yet few were willing to inject the TAP50 solution, and none were willing to inject the TAP250 solution.

Relative Perceived Monetary Value and Removing Unwanted Particles—Table 10 demonstrates that almost all of the sample would pay “Less” for a tablet that that took more time and effort to prepare than one that was quicker and easier to prepare. The remainder (<10%) would pay the same for both tablets. None would pay “More.” Lastly, Table 11 reveals that all of the participants took precautions to avoid unwanted particles from ending up in extractions that they typically prepared for use.

Discussion

Two studies were conducted to determine whether the TAP formulations were able to be manipulated by experienced intranasal and intravenous OxyContin® abusers. OxyContin®

40 mg was used as a comparator. The results from both studies revealed differences between the TAP and OXY40 formulations across almost all of the measures assessed.

Few individuals were willing to snort the particles or inject the solutions produced from the TAP tablets. With regard to the particle sizes, fewer particles were generated from the TAP tablets and, on average, were larger than those produced from OXY40. A previous study estimated that particles up to 285.9 μm would easily be intranasally administered [38]. Thus, the current data suggest that greater than 96% of the TAP tablets may consist of particles too large to be considered for snorting. This is notable in view of the observation that half of those who indicated they would snort the remnants of their tampering attempts used water to prepare a solution to use as drops. Lastly, there was a 10-fold increase in the percent yield of active drug recovered from OXY40 in comparison with TAP50 while no drug was able to be recovered from the TAP250 samples, primarily due to the fact that none of the TAP250 samples returned from analysis were in a liquid state; all were gelled.

In addition to these differences between formulations, this data set affords a consideration of tampering behaviors. Participants were given an hour to tamper with each tablet in the present studies, yet none of the intranasal abusers approached the 60-minute time frame. The average time spent preparing the OXY40 was 3 minutes compared to 6 minutes for TAP50 and 7 minutes for TAP250. One participant spent a maximum of 21 minutes preparing a TAP50 tablet. More meaningfully, however, the median preparation time for intranasal abuse across the sample was 4.6 minutes (versus a median of 2.5 minutes for OXY40, and 7.3 minutes for TAP250). Similarly, the maximum time employed by an intravenous abuser working with a TAP250 tablet was 48.9 minutes, yet the median preparation time for the TAP250 was 7.3 minutes (versus 5.7 minutes for OXY40 and 6.8 minutes for TAP50). Thus, although they indicated they were willing to spend more time preparing the TAP tablets, most intravenous and intranasal abusers did not spend a great amount of time tampering with any of the tablets [23, 27, 39–40].

As has also been found [38], no particularly unique tools were requested for tampering purposes. Intranasal abusers worked primarily with a hammer, razor, or dollar bill; while intravenous abusers primarily employed a lighter, spoon, syringe, cotton, and water. This is consistent with observations gleaned from the internet regarding tampering, namely, complex procedures are not typically employed by substance abusers to tamper with medications [41–42].

One question that surrounds the TRFs is their effectiveness towards abuse-deterrence in a population known for extraordinary creativity and determination. Taken together with another similar published study to-date [38], these data suggest that approximately 14% of intranasal abusers (range 8%-20%) will attempt to snort them, and 18% of intravenous abusers (range 16%-20%) will attempt to inject them. This implies that up to 86% of intranasal abusers, and up to 82% of intravenous abusers may experience some deterrence from these formulations. Whether or not these estimates bear out in larger samples remains to be seen; however, these data are encouraging towards the employment of this technology.

It is not known what will happen if an individual snorts the powder, or more problematically, injects the extracts from these formulations [see summary in 38]. These risks should not be underestimated [43–50]. It is encouraging that all individuals in this sample indicated that they removed unwanted particles from their drug extractions, and 48% indicated this was due in some part to safety or not wanting foreign materials in their bodies. Whether or not this logic extends to the extracts from the INTACTM matrix remains to be seen. Future research should locate substance abusers who have abused or attempted to

abuse these formulations because they may be more proficient at bypassing the matrix and extracting active drug.

With regard to this study, the findings must be considered in the context of the present limitations. It is possible that the recruitment of OxyContin® or oxycodone abusers confounded the study results, notably because the OXY40 tablet may have been preferred due to familiarity. However, only eight participants in each study reported abusing the OXY40 tablet; the remainder used other doses. This was reflected in the results: while some IN and IV abusers indicated that they preferred the OXY40 due to the product recognition, a larger number indicated that their preference was due to the form, or the production process of the powder or solution (reported in Tables 3 and 9). Further, in a comparable study [38], there were no restrictions placed on the type of prescription opioids being abused by participants, and similar results were generated. This suggests, at minimum, that familiarity was not the only driving force in participants' preferences. Much of the data collected were self-reported, which leaves open the possibility that when faced with an immediate opportunity to snort or shoot a tampered product, a different decision would actually be made. It is also possible that if participants had some time to think about the products after the sessions, they would have generated strategies. To this end, follow-up phone calls the day after the session might have revealed more information. A direct comparison to another formulation that has been designed to be tamper-resistant would have provided useful information with regard to relative ease of tampering with different products, however, none were available during the conduct of these procedures. This would be an interesting follow-up study to pursue.

To conclude, data from Studies 1 and 2 suggest that the abuse-deterrent formulations of tapentadol reduced the ability of both intranasal and intravenous abusers to quickly and successfully tamper with this medication when compared to the non-tamper-resistant OxyContin® formulation. These findings were captured in the quantitative data that were generated, as well as the participants' qualitative perceptions of their experiences. It seems reasonable to conclude that even when considering the potential safety concerns, tamper-resistant tablets are a promising technology for reducing the intranasal and intravenous abuse of prescription opioids.

Acknowledgments

The authors gratefully acknowledge Janet Murray, R.N., Claudia Tindall, N.P., Sharifa James, Greta B. Raglan, Joseph Lazar, Phillip Saccone, Elias Dakwar, M.D., Shanthi Mogali, M.D., David Mysels, M.D., and Rebecca Pyle for their assistance with the execution of the study. In addition, two anonymous reviewers provided valuable feedback on an earlier version of this manuscript. This study was supported by Johnson and Johnson PRD, LLC.

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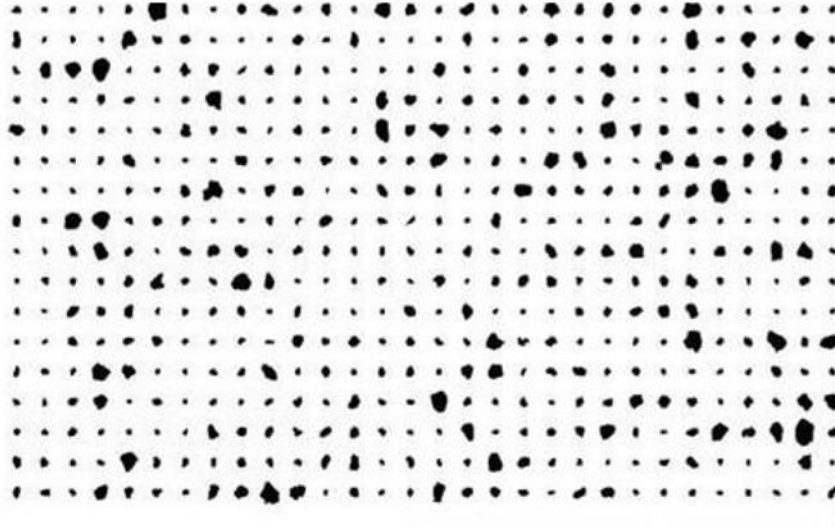
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Figure 1. Top Panel: Intranasal particles produced from the OXY40 (A), TAP50 (B) and TAP250 (C) tablets; Bottom Panel: Intravenous solutions/gels produced from the OXY40 (D), TAP50 (E) and TAP250 (F) tablets.

A. OxyContin® 40 mg



B. Tapentadol crush –resistant formulation

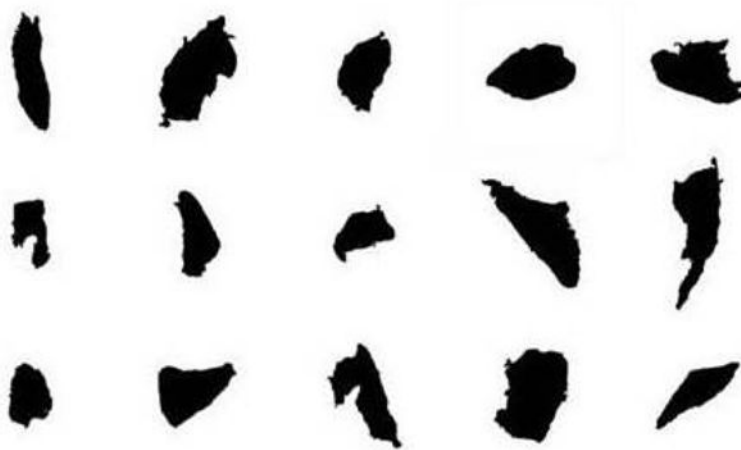


Figure 2.
HSIA particle sizes to scale

Table 1

Demographics

	Study 1, n=25 (Intranasal)	Study 2, n=25 (Intravenous)
Age, M(SD)	42 (11)	41 (9)
Gender, % Male	72	84
Ethnicity, %		
Black	44	4
Hispanic	36	36
White	16	56
Mixed	4	4
Education, % with some college	52	72
Age of first OxyContin® use, M(SD)	37 (11)	34 (10)
Length of OxyContin® use in yrs, M(SD)	5(4)	6 (5)
Current Drug Use, %		
Oxycontin® or generics	100	100
Heroin	56	96
Benzodiazepines	48	16
Cocaine	36	20
Methadone	36	8
Alcohol	8	16
Marijuana	0	16
Ecstasy	4	0
PCP	4	0
Quaaludes	4	0
Percocet™	0	8
Vicodin™	0	8
Morphine	0	8
Tylenol with Codeine #3™	0	4
Crystal Methamphetamine	0	4

Table 2
Tools and Solvents Used for Intranasal (Left) and Intravenous (Right) Drug Preparation

Intranasal Tools	n	(%)	Intravenous Tools	n	(%)
Hammer	22	(88)	Lighter	25	(100)
Razor	21	(84)	Spoon	25	(100)
Dollar Bill	9	(36)	Syringe	25	(100)
Paper	7	(28)	Hammer	23	(92)
Lighter	6	(24)	Cotton/Cotton pads	23	(92)
Paper Towels/Napkins	6	(24)	Razor	20	(80)
Credit Card/ID Card/MetroCard	4	(16)	Paper Towel/Napkin	15	(60)
Spoon	4	(16)	Paper	12	(48)
Wax Paper	4	(16)	Dollar Bill	9	(36)
Pill Grinder	3	(12)	Knife/Exacto Knife	7	(28)
Quarter/Coins	3	(12)	Wax Paper	6	(24)
Screwdriver	3	(12)	Pliers	3	(12)
Strainer	3	(12)	Quarters/Coins	3	(12)
Syringe/Plastic Syringe	3	(12)	Coffee Grinder	2	(8)
Pen Knife/Knife/Exacto Knife	2	(8)	Screwdriver	2	(8)
Pill Crusher	2	(8)	Strainer	2	(8)
Pliers	2	(8)	Glass vial	1	(4)
Bottle Opener	1	(4)	Mortar & Pestle	1	(4)
Cotton	1	(4)	Paper Clip	1	(4)
Matchbox	1	(4)	Plastic Cap	1	(4)
Scissors	1	(4)			
Straw	1	(4)			
Solvents	n	(%)	Solvents	n	(%)
Water	6	(24)	Water/Saline	25	(100)
Alcohol Pads	1	(4)	Lemon Juice	1	(4)

Table 3

“If given the opportunity to snort the powder that you made, would you do it? Why?”

	OXY40 (%)	TAP50 (%)	TAP250 (%)
Would snort the product	100	24	16
■ Form: In a form that would snort/nice, fine powder/small enough/powdery form/in form would use	44		
■ Process: Easy to crush/able to get small enough/easy to grind/takes minimal time	36		
■ Recognition: Know it's Oxy/like it/looking for high	20		
■ Dissolving possibility: Would dissolve for nose drops/would use water to wash down nostrils		16	8
■ Particle size: Particles are small enough		8	8
Would not snort the product	0	76	84
■ Form: Cannot snort/too dense/too large/hard as a brick/too sticky/unbreakable/plastic-y/not powdery/rough/pill not real		36	40
■ Process: Not able to make/too difficult to turn into powder/requires too much time/too much work/too process consuming/not crushable		40	44

Table 4

Particle Size Analysis

	OXY40					TAP50					TAP250					
	n	M	SD	Med	n	M	SD	Med	n	M	SD	Med	n	M	SD	Med
% Tablet weight (wgt) recovered	24	68.9	11.2	70.6	25	96.2	9.2	99.5	25	93.3	14.7	98.8				
% Recovered tab wgt > 850 µm	24	20.8	21.1	15.6	25	97.9	7.1	100.0	25	98.7	4.6	100.0				
% Recovered tab wgt < 850 µm	24	79.2	21.1	84.4	25	2.1	7.1	0.0	25	1.3	4.6	0.00				
# Particles measured by H5IA	23	41,595	24,269	38,080	8	1,337	1,917	440	9	1,818	2,252	969				
Pairwise Comparisons																
		TAP50 vs. OXY40					TAP250 vs. OXY40					TAP50 vs. TAP250				
		LS Mean Difference	95% CI			LS Mean Difference	95% CI			LS Mean Difference	95% CI			LS Mean Difference	95% CI	
% Tablet wgt recovered		27.1**	(21.4 to 32.9)			24.2**	(18.4 to 29.9)			-2.9	(-8.6 to 2.7)			-2.9	(-8.6 to 2.7)	
% Recovered tab wgt > 850 µm		77.0**	(69.8 to 84.2)			77.8**	(70.6 to 85.0)			0.8	(-6.3 to 7.9)			0.8	(-6.3 to 7.9)	
% Recovered tab wgt < 850 µm		-77.0**	(-84.2 to 69.8)			-77.8**	(-85.0 to -70.6)			-0.8	(-7.9 to 6.3)			-0.8	(-7.9 to 6.3)	
# Particles measured by H5IA		-31,878**	(-44,041 to -19,725)			-32,878**	(-44,483 to -21,274)			-1000.4	(-13,679 to 11,678)			-1000.4	(-13,679 to 11,678)	

M=Mean, SD=Standard Deviation, Med=Median

** p<.001

Table 5

Time Participants Spent Preparing Tablets for Intranasal Abuse, and Self-Reported Maximum Time Participants Would Spend Preparing Tablets for Intranasal Abuse

	Actual Time Spent Preparing Tablets (minutes) ¹		Maximum Time Would Spend Preparing Tablets (minutes) ²			
	M	SD	Range	M	SD	Range
OXY40	2.9 ^{**}	1.9	0.7 to 8.8	4.8 [*]	4.8	1.0 to 15.3
TAP50	5.9 ^{**}	4.9	0.9 to 20.9	10.8 [*]	12.7	0.0 to 28.7
TAP250	7.1 ^{**}	4.6	0.9 to 16.2	11.6 ^{**}	12.5	0.0 to 48.9

M=Mean, SD=Standard deviation

^{**} p<.01;

^{*} p<.05, TAP50 vs. OXY40, and TAP250 vs. OXY40

¹F(2, 24)=9.55, p=.0003;

²F(2, 24)= 6.60, p=.003.

Table 6

“For a tablet that takes substantially more time and effort to prepare for snorting, would you pay LESS, MORE, or THE SAME than for a tablet with the same drug in it that is quicker and easier to prepare?”

	Less (64%)	The Same (36%)	More (0%)
■ Could not manipulate tablet: Can't snort/can't make into powder/not worth it if in withdrawal	24		
■ Preparation time: Time matters/takes more time/would take longer	16		
■ Effort required: Difficult pill/requires more effort/won't have same effect/harder to prepare	16		
■ Particle qualities: Particles/too large/texture gummy/would take orally	8		
■ Buying the drug, not the formulation: High from TRF may be better even though more work/paying for drug/if same effect, same price		32	
■ New ideas: Would think of new way to prepare pill		4	

Cochran's Q (2) = 24.13, $p < .01$; "Less vs. More," $p < .05$

Table 7

“When you prepare an OxyContin® tablet for snorting, how often do you take measures to prevent unwanted particles from ending up in the powder?”

	%
Always	52
▪ Removes coating first: Cracks and removes shell/uses alcohol (before mixing with heroin)/sucks coating off/coating irritates stomach	28
▪ Uses filter: Cotton filter/metal strainer	8
▪ Particles: Doesn't want foreign particles in nose/won't snort with large pieces	8
▪ No answer	8
Usually	16
▪ Depends: If has dark shell will remove, otherwise won't/if coating comes off easily will remove, otherwise won't/sometimes too sick to bother	8
▪ Removes coating first: Cracks and removes shell/uses alcohol (before mixing with heroin)/sucks coating off/coating irritates stomach	4
▪ Snorts everything, including coating: Usually snorts all of the remnants	4
Sometimes	12
▪ Snorts everything, including coating: Usually snorts all of the remnants	4
▪ Depends: If has dark shell will remove, otherwise won't/if coating comes off easily will remove, otherwise won't/sometimes too sick to bother	4
▪ No answer	4
Never	20
▪ Snorts everything, including coating: Usually snorts all of the remnants	20

Table 8

Time Spent Preparing Tablets for Intravenous Abuse, and Self-Reported Maximum Time Participants Would Spend Preparing Tablets for Intravenous Abuse

	Actual Time Spent Preparing Tablets (minutes)		Maximum Time Would Spend Preparing Tablets (minutes)			
	M	SD	Range	M	SD	Range
OXY40	6.57	3.16	2.75–15.27	15.22	18.03	0.00–60.00
TAP50	8.27	7.60	1.15–28.67	17.66	20.23	0.00–60.00
TAP250	10.58*	9.68	1.53–48.85	22.52	40.53	0.00–180.00

M= mean, SD = standard deviation.

F(2, 48) = 3.08, p=.055;

* p<.05, TAP250 vs. OXY40

Table 9

“If given the opportunity to inject the extract (the solution) that you made, would you do it? Why?”

	OXY (%)	TAP50 (%)	TAP250 (%)
Would inject the solution	100	16	0
▪ Form: Acceptable/can inject in current form	32		
▪ Process: No problem breaking up/could crush and cook/easy to draw up/easy to extract	32		
▪ Recognition: It's Oxy/it's an opiate/know what it is	24		
▪ Effort: Minimal effort/minimal time required	12		
▪ Solution consistency: Clear/not sticky/has drug in it		12	
▪ Effort invested: Because spent so much time preparing		4	
Would not inject the solution	0	84	100
▪ Form: Couldn't get into form/won't break up/can't cook/not breaking down/not melting/not dissolving		40	36
▪ Solution consistency: Jelly/rubbery/plastic/gummy/gel-like/goosey/syrupy		24	44
▪ Risks: Dangerous/scared about veins/scared about potential abscesses		12	8
▪ Recognition: Don't know what it is/not a pill/unfamiliar/pill is oily/pill is rubbery		8	12

Cochran's $Q(2) = 38.17$, $p < .001$; OXY40 vs. TAP50 $p < .01$; OXY40 vs. TAP250, $p < .01$; TAP50 vs. TAP250, NS.

Table 10

“For a tablet that takes substantially more time and effort to prepare for injection, would you pay LESS, MORE, or THE SAME than for a tablet with the same drug in it that is quicker and easier to prepare?”

	Less (92%)	The Same (8%)	More (0%)
■ Requires more work: Harder to break up/too hard/aggravating	32		
■ Can't use: not sure can prepare/can't break it down/would break needle/can't use in a syringe/can't use	32		
■ Too time consuming: takes too long – especially if desperate/not worth the risk of getting caught	28		
■ Need: If wanted it bad enough, would pay the same		4	
■ Economics: wouldn't pay more, dealer won't sell for less		4	

Cochran's Q (2) =42.35, p<.001; “Less vs. The Same,” p<.01; “Less vs. More,” p<.01

Table 11

“When you prepare an OxyContin® tablet for intravenous injection, how often do you take measures to prevent unwanted particles from ending up in the extraction?”

	%
Always	100
▪ Removes shell first: Peels pill/removes coating with damp cloth/shaves shell/sucks shell off) then filters with cotton	44
▪ Uses Cotton: cotton balls/cigarette filters to keep particles out/filter out excess particles/doesn't want foreign material	32
▪ To avoid infection: avoid dangerous particles in body/blood/avoid abscess/prevent illness	16
▪ Clean solution: to avoid clogging needle/wants clean fluid	8