

Innovative formulation technology

Protecting intended drug action



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The Problem of Prescription Drug Abuse

"Prescription pills are East Tennessee's 'new crack'"

Knoxville News Sentinel

EPIDEMIC: RESPONDING TO AMERICA'S PRESCRIPTION DRUG ABUSE CRISIS:

"The latest Monitoring the Future study—the nation's largest survey of drug use among young people—showed that

Prescription drugs are the second most-abused category of drugs after marijuana."

University of Michigan, 2009, Monitoring the Future: A Synopsis of the 2009 Results of Trends in Teen Use of Illicit Drugs and Alcohol

"Drug Is Harder to Abuse, but Users Persevere"

New York Times

Misuse and Abuse

Prescription opioids are at the center of a major public health crisis of misuse and abuse in the United States. The most recent data from the National Survey on Drug Use and Health, conducted annually by the Substance Abuse and Mental Health Services Administration (SAMHSA), revealed that nearly one-third of people aged 12 and over who used drugs for the first time in 2009 began by using a prescription drug non-medically.¹ A 2011 study, also conducted by SAMHSA, showed a heavy increase in the number of admissions to substance abuse treatment facilities nationwide for prescription drug abuse.² The proportion of admissions of those aged 12 and older involving abuse of prescription opioids had risen by over 400 percent from 2.2 percent in 1998 to 9.8 percent in 2008.



Figure 1a: Conventional tablet crushed between two spoons

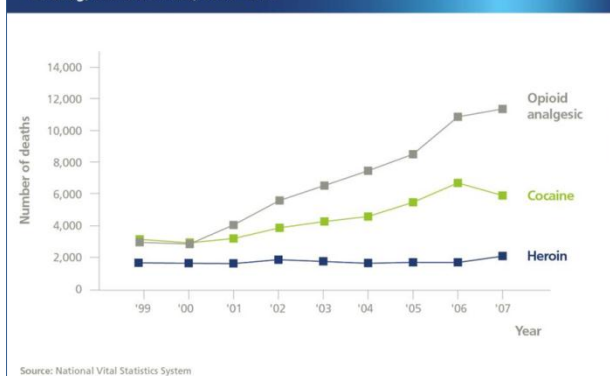
For the past several years, numerous investigators and pharmaceutical companies have been working diligently to come up with technological solutions to make it more difficult for abusers to tamper with prescription opioid products. Table 1 provides a general overview of approaches for abuse deterrence, pairing the technological approach with the route of abuse (ROA) it is intended to deter.

Prescription opioid abuse is now labeled an "epidemic" by the Center for Disease Control³ as well as the White House, the latter of which in its 2011 "Prescription Drug Abuse Prevention Plan" calls on the National Institute on Drug Abuse and the FDA to support efforts for the development of abuse-deterrent formulations of opioid medications and other drugs with abuse potential.⁴ This is because many prescription opioid products are available in formulations which are easily converted from their intact tablet or pill formulation into a form which allows abuse by other routes such as snorting and injecting.



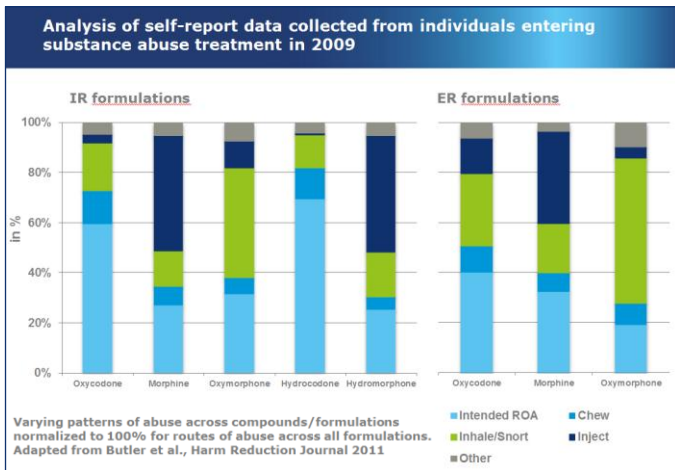
Figure 1b: Conventional tablet crushed in Pill Crusher

Unintentional drug overdose deaths by major type of drug, United States, 1999–2007



The Problem of Prescription Drug Abuse

How Different Opioids are Abused



Technologies Intended to Hinder Different Routes of Abuse

Approach/ Route of abuse	Multiple doses, swallowing intact	Chewing	Snorting	Injecting
Niacin				
Emetic				
Pro-drug				
Bittering agent				
Dye				
Capsaicin				
Naloxone				
Naltrexone (sequestered)				
Gelling				
Hardness				

Table 1: Intentions of various technological approaches to deter abuse⁵

FDA officials have stated that the development of abuse deterrent technologies is encouraged and must demonstrate a high level of quality.⁶ In order to choose the best formulation that would have the potential to effectively reduce the abuse of a given product, it is necessary to understand by which ROA(s) that particular product is being abused. An analysis of 2009 substance abuse treatment admissions, published by Butler et al. in 2011,⁷ examined not only the prevalence of abuse of various prescription opioids, but also the routes of abuse (ROA) employed by this population.

Whether IR or ER, prescription opioid products which are pure opioids have a high prevalence of being abused by routes which first require the crushing of the tablet or pill.

Therefore, a tamper-resistant formulation which makes these products more difficult to crush would be expected to reduce the prevalence of abuse of these products by chewing, snorting, and injecting. In August 2010, a reformulated "crush-resistant" OxyContinTM was introduced to the US market.

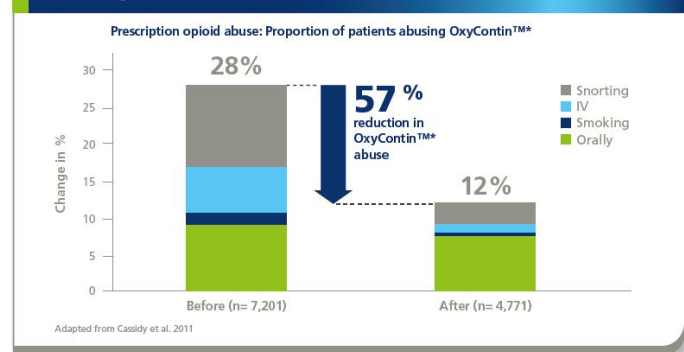
Impact of TRFs: Emerging Evidence in the Real World

Not only was there a decrease in the abuse of prescription opioids by non-oral routes, but there was also a 57% reduction in the overall abuse of OxyContinTM by the prescription opioid abusers entering these treatment centers, providing some of the first "real-world" evidence that a tamper-resistant formulation can play an important role in reducing the abuse of prescription opioids.



Figure 2: Conventional tablet cut with kitchen knife

Figure 3: Shift in ROA of OxyContinTM following reformulation



*Reformulated OxyContinTM uses technology to address abuse potential – not INTACTSM

References

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