Category 1 Assessment: Vaping of Abuse Deterrent Opioid Formulations

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Introduction

- The use of e-cigarettes, also called vaping and more recently "JUULing", is a well documented method used to administer nicotine and cannabis products.
- In 2014, teenage use of vaping devices surpassed that of smoked cigarettes and its prevalence continues to increase across all age groups.
- Although e-cigarettes are not designed with the intent to administer opioid drug products the success of newer e-cigarettes brands and technologies in administering alternative cannabis forms such as herbal, wax and concentrates, indicates other material forms, like ground opioid formulations, might be possible.
- Some laboratory studies with rodents have reported success with other drug classes, e.g., methamphetamine, MDPV, alpha-PVP (Marusich et al., 2016).
- Online drug tampering forums mention vaping marketed opioid formulations however, the success of such attempts is mostly undetermined.
- Questions have been posed by FDA Advisory Committee members regarding the potential for vaping opioids. To address the feasibility of e-cigarette devices to successfully deliver opioids, a laboratory model was developed and tested with pure oxycodone, a marketed abuse deterrent (AD) formulation, and non-abused deterrent (NAD) formulation of oxycodone.

Methods

A laboratory model was assembled that consisted of a commercial vaping device connected to an air vacuum sampling bag and flow meter control. A preliminary optimization and verification procedure was conducted using pure oxycodone hydrochloride (HCl) diluted to a total volume of 2 mL with 50:50 propylene glycol/vegetable glycerin; for a final concentration of 10 mg/mL in the vaping concentrate.

The vaping device was set to "VW" mode and 100 watts; causing the device to set the maximum watts and automatically apply voltage to avoid damage to the heating coil. The flow rate of air passing through the device was allowed to equilibrate to a range of 1800 – 2500 mL/min, typical of a human inhalation rate. Once the flow rate reached an acceptable range, the vaping device was turned on for 5 seconds, off for 2 seconds, and then back on for 5 more seconds.

A total of 6 vaping cycles (5 sec – 2 sec – 5 sec) were collected individually using a single concentrated vaping solution. A total of 4 were performed during optimization with pure oxycodone HCl. The vacuum flow was left on until the vapor ceased and then the tubing was immediately introduced into 200 mL of collection solvent, thus rinsing the inside of the vapor tubing and collecting the oxycodone residue in the air sampling bag.

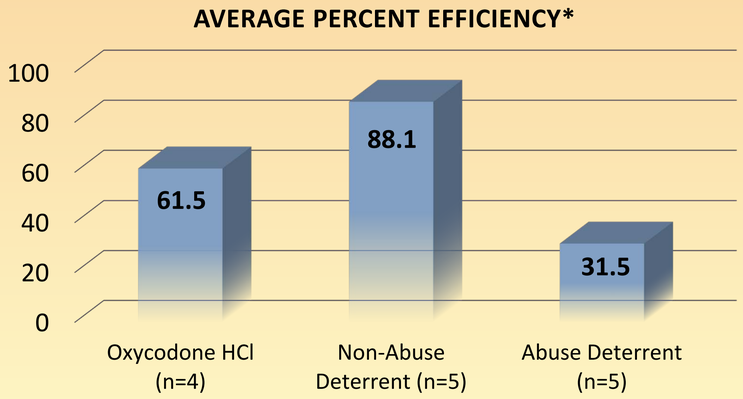
The contents of each sampling bag were analyzed by LC-MS/MS for total oxycodone recovery.

Methods (cont'd)

- Experiments involving non-abuse deterrent tablets were extracted 24 hours at room temperature into 4 mL of tap water, filtered with a 10 μm syringe filter, and reduced to ~ 400 μL to concentrate the solution.
- Experiments involving an abuse deterrent tablet required a 3-5 minute thermal extraction and concentration process to yield a concentrated solution of oxycodone, without significant tablet excipient and gelling.
- The resulting tablet extracts were diluted to a final volume of 2 mL with 50:50 propylene glycol/vegetable glycerin; for a final concentration of approximately 10 mg/mL.
- The vaping procedure optimized using pure oxycodone HCl was applied and further optimized for the formulation derived vaping concentrates. Optimization revealed that 100W was too aggressive and caused burning of the coil. Wattage was optimized at 35W for the formulations.

Results

- Results from optimization and verification of the laboratory model showed successful vaporization of oxycodone HCl in the range of 1.6 – 2.2 mg.
  - When this API measurement is taken in context of the total volume of vaping concentrate vaped, mass difference pre versus post vaping, approximately 57-63% (efficiency) of the oxycodone HCl was successfully transferred to the collection bag.
  - The method was very consistent as shown by a CV < 6%.
- Results from the oxycodone formulations were averaged 88.1% for NAD and 31.5% AD.
  - The method was very consistent as shown by a CV of 9% for NAD and 6% for AD.
  - Of note, the first vape cycle with the formulations was disregarded as this cycle was necessary to prime and saturate the heating coil.



$$Efficiency = \frac{mg\ oxycodone\ vaped}{theoritical\ API\ vaped\ calculated\ from\ volume\ loss}$$

Specialized Materials

- Defender 510 flow meter
- 1/8" x ¼", 3/8" x ½", ¼" x 7/16" tubing
- 60 mL syringes Bulkware
- Smok- G-priv kit Vapoizer
- Smok v8 baby-M20.25 ohms atomizers
- Vegetable Gylcerin Essential Depot
- Propylene Glycol Food Grade
- Chemotronics Swabs
- Gas sampler and gas sample bags (0.5L)

Conclusion

- Based on this study, a laboratory model and process was developed that successfully utilized a commercial vaporizer to deliver oxycodone vapor (aerosol) derived from a marketed non abuse deterrent formulation and an abuse deterrent formulation in amounts likely to produce pharmacological effects.
- Given the trending popularity of vaping as a means of drug delivery (nicotine, cannabis), it is feasible that this laboratory method will be realized in the "real-world" to successfully administer and conceal opioid abuse.
- Based on previous work performed at Drugscan, this method of vaporization is significantly more feasible than traditional smoking methods utilizing flames and direct heat sources. In such traditional methods, vaporizing of oxycodone ranges from failure (0%) to 10%.
- In vitro experiments were limited to just 6 vaping cycles with approximately 75% of the concentrated vaping solution remaining. Theoretically, an abuser could vape the entire contents for ~30-40% of the entire dose content.

References

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Financial Disclosures

None. In the interest of transparent disclosure, PinneyAssociates (PA) works on an exclusive basis on smoking cessation and tobacco harm minimization products (such as vaping devices) and issues with Reynolds American Inc (RAI). PA does not work on RAI's conventional cigarettes.

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