Use of Dissolution to Characterize and Compare Oral Nicotine Products

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Abstract

The market for oral tobacco pouches has been increasing in recent years as adult tobacco consumers are seeking alternatives to traditional tobacco products. The use of oral tobacco products is considered by many to reduce risks of harm caused by smoking cigarettes. Nicotine pouches that do not contain tobacco leaves have emerged as a new category of oral tobacco products. These oral tobacco-derived nicotine (OTDN) products are pre-portioned pouches similar to snus, except that the tobacco leaf is replaced with non-tobacco filler and food grade ingredients. Since the nicotine in the OTDN is added, there are several questions about its release from the pouch. We utilized dissolution test systems to measure the release of nicotine to characterize and compare oral tobacco products.

To determine the nicotine release profile of BIDI® Pouch compared to other pouch products, the FDA's Guidance for Industry was followed throughout the testing and comparison process. We tested three BIDI® Pouch flavors and three comparator products.

The nicotine release profile of three BIDI® Pouch flavors and three comparator products, including General Snus, were determined using the FDA's Guidance for Industry, Dissolution Testing of Immediate Release Solid Oral Dosage Forms.

Similar to Swedish Match General Snus, BIDI® Pouch products released 38% of the total pouch nicotine at 20 minutes. The two other comparator products released ~90% of the total pouch nicotine at 20 minutes. The similarity of the BIDI® Pouch release to Swedish Match Snus is important for three reasons. First, BIDI® Pouch products are the only OTDN products in this study that deliver nicotine like a tobacco containing pouch. Second, Swedish Match is authorized by the FDA to market and make reduced exposure claims about its snus products. Finally, as the BIDI® Pouch products nicotine release closely replicate the Swedish Match General Snus, it could be inferred that the pharmacokinetic profiles would be similar as well.

Our results support the use of dissolution testing to characterize and compare oral tobacco products with potential bridging for pharmacokinetic parameters.

Background

Dissolution testing is designed to measure the release of nicotine from OTDN pouches for product characterization and product-to-product comparisons.

Dissolution testing is commonly used by the pharmaceutical industry to assess product quality, demonstrate equivalency in constituent release, guide formulation design, and development [1]. Dissolution testing measures *in vitro* drug release as a function of time. This may reflect the reproducibility of the manufacturing process and, in some cases, relates to the active ingredients release into the body [2].

To determine the nicotine release profile of BIDI® Pouch products compared to other pouch products, over a 60-minute time period, we submitted several products to Enthalpy Analytical, LLC for dissolution testing. We used the FDA's Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms as guidance throughout the testing and comparison process.

Method

The Enthalpy method is for the determination of nicotine in dissolution media and analyzed by ultra-high performance liquid chromatography using UV detection. Note for this method, the term dissolution media generally refers to artificial saliva or other aqueous salt media.

The method is applicable to the quantitation of nicotine in dissolution media that has passed through smokeless tobacco or other oral nicotine products during a dissolution collection. The limit of quantitation for this method is 0.05 ug/mL.

An aliquot of dissolution media is transferred to an amber autosampler vial. Following the addition of internal standard, samples are diluted with artificial saliva. The vial is capped and mixed prior to analysis via UPLC- UV.

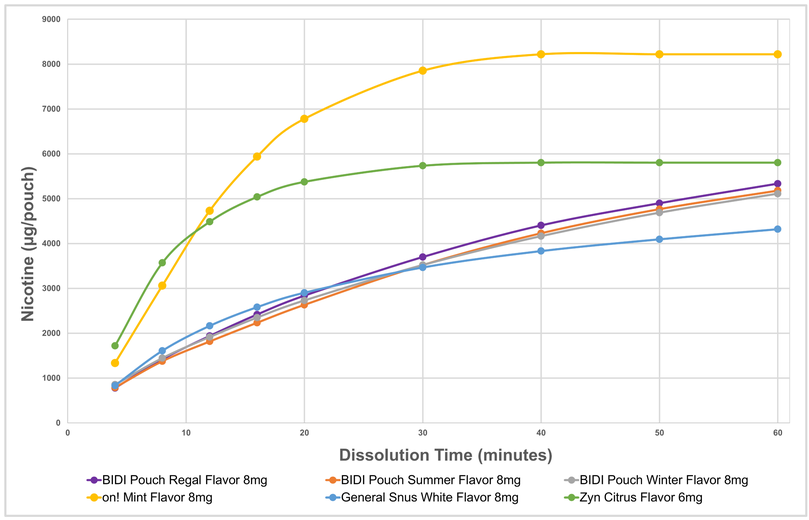
Results

- **BIDI® Pouch released 38% of total pouch nicotine at 20 min and 68% at 60 minutes.**
- **General Snus released 38% of total pouch nicotine at 20 min and 40% at 60 minutes.**
- **BIDI® Pouch products is the only OTDN product that delivered nicotine like a tobacco containing pouch product (e.g., Snus).**
- **On!® released 91% of total pouch nicotine at 20 minutes and at 30 minutes no additional nicotine was released.**
- **Zyn released 87.5 % of total pouch nicotine at 20 minutes and at 30 minutes no additional nicotine was released.**

Table 1 Product Dissolution Rate Comparison

Product	% per Minute
BIDI® Pouch Regal Flavor 8 mg	**1.67**
BIDI® Pouch Summer Flavor 8 mg	**1.67**
BIDI® Pouch Winter Flavor 8 mg	**1.67**
On!® Pouch Mint Flavor 8 mg	**2.50**
General Snus White Flavor 8 mg	**1.67**
Zyn Pouch Citrus Flavor 6 mg	**2.50**

Figure 1 Cumulative release profiles of nicotine collected from all pouches at 8 and 6 mg nicotine



Study Summary

Three replicate collections were performed for each of the six samples. Each collection incorporated nine fractions totaling a combined twenty-seven replicates per sample. All replicates for each brand were performed on the same day. All applicable analytical methods have been fully validated. All sample analyses performed were conducted on site using the Dissolution Apparatus method previously described.

Observations & Conclusions

- BIDI® Pouch releases nicotine similarly to Swedish Match's General Snus an FDA authorized modified risk tobacco product.
- Zyn® and on!® released the majority of their nicotine within 20 minutes. Adult tobacco consumers are likely to enjoy General Snus and BIDI® Pouch longer than one hour due to prolonged release of nicotine.
- The dissolution results suggest that nicotine release rates for BIDI® Pouch are equivalent to General Snus. Therefore, BIDI® Pouch is likely to provide a similar nicotine exposure profile and have similar abuse potential as an FDA Authorized product.
- Further studies are need to determine the complete nicotine release for BIDI® Pouch.

References

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