

DISSOLUTION TESTING OF A NOVEL NON-TOBACCO LONG CUT AND POUCH NICOTINE PRODUCT

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ABSTRACT

Smokeless tobacco products contain TSNAs and other HPHCs. Black Buffalo Inc. has designed a novel smokeless product that is based on a common non-tobacco agricultural commodity. The non-tobacco leaf is cured and processed like tobacco but does not contain TSNAs or PAHs. Tobacco derived nicotine is added to the processed leaf. The products are available in two forms: loose (Long Cut) and fleece-portioned (Pouches). The filler material inside the Pouches products is the same as that used for the Long Cut products. Black Buffalo's products are designed to emulate the organoleptic, ritualistic, and pharmacokinetic aspects of traditional smokeless products. The Black Buffalo products and two market comparators Copenhagen Long Cut Wintergreen and General Snus Wintergreen Portion White Large were tested by using methods similar to those described for dissolution testing of pharmaceuticals. The USP-4 apparatus was used with artificial saliva. Samples of all the study products were placed in the apparatus flow-through cells at a constant temperature of 37°C. A pump delivered a constant flow of artificial saliva for 100 minutes. The flow was sampled throughout the release period. The method followed the approach of Miller et al. 2020. The dissolution rate was faster for the Long Cut products (5% per minute) as compared to 1.67% per minute for the Pouch products. The dissolution extent (mg/unit) was similar for the Black Buffalo Long Cut products (range 7.1 to 9.2) as compared to Copenhagen Long Cut (8.7). The dissolution extent for the Black Buffalo Pouches was similar to the Long Cut products (7.8 – 8.7) but greater than the General Snus market comparator (4.4).

OBJECTIVE

Determine the release profiles of the novel products and compare them to market comparators, General Snus Wintergreen Portion White Large and Copenhagen Long Cut Wintergreen.

THE PRODUCTS

Black Buffalo's tobacco alternative products were developed as an alternative to traditional MST products, with the intent of eliminating user exposure to the TSNAs and PAHs found in traditional MST products. Black Buffalo (BB) products are made by applying food-grade flavors, pharmaceutical-grade tobacco-derived nicotine, salt, water, preservatives, humectants, and pH modifiers to a food leafy vegetable that have been flue-cured (i.e., dried using indirect heat), cut, and processed into a low-moisture biomass that resembles finely shredded tobacco.

The products do not contain any tobacco leaf or tobacco stem material, but they do contain tobacco derived nicotine and are intended to emulate the organoleptic, ritualistic, and pharmacokinetic aspects of traditional moist smokeless (MST) products. The products are intended to be placed in the mouth between the cheek and gum for a period of time determined by the user (typically 30 to 60 minutes).

Black Buffalo's Long Cut and Pouches Tobacco Alternative Products

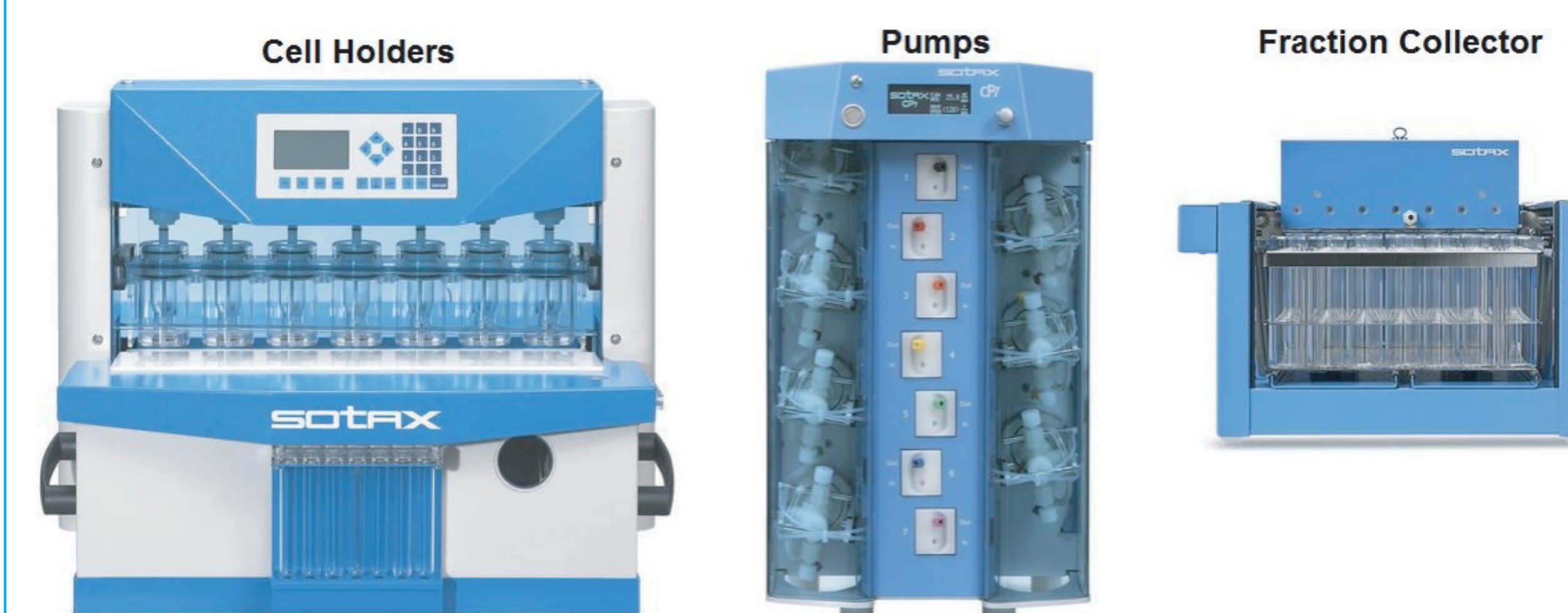


Table 1. Product Flavors

Product Name	Nicotine Concentration
Black Buffalo Wintergreen Long Cut	7.5 mg/g
Black Buffalo Mint Long Cut	7.5 mg/g
Black Buffalo Straight Long Cut	7.5 mg/g
Black Buffalo Peach Long Cut	7.5 mg/g
Black Buffalo Blood Orange Long Cut	7.5 mg/g
Black Buffalo Wintergreen Pouches	11.25 mg / portion
Black Buffalo Mint Pouches	11.25 mg / portion
Black Buffalo Straight Pouches	11.25 mg portion

METHODS

The products and two market comparators were tested using methods similar to those described for dissolution testing of pharmaceuticals. The USP-4 flow-through cell apparatus in an open loop offline configuration with large cells (22.6 mm diameter) was used with artificial saliva. Artificial saliva was prepared according to the method provided by Pickering Labs (De Caro et al.) Samples of all the study products were placed in the apparatus flow-through cells at a constant temperature of 37°C. A pump delivered a constant flow of artificial saliva for 100 minutes. The flow was sampled throughout the release period. The method followed the approach of Miller et al. 2020 . The Dissolution Apparatus is shown in below: SOTAX CE7 Smart Flow Through System



RESULTS

Table 1 shows the amount of nicotine extracted and pH of the products in artificial saliva.

- Approximately 80% of the total nicotine is bioavailable and being released from the BB Products
- Release from comparator products was similar
- The degree of protonation ranged from 41% to 53% for the BB Products, while General Snus was 96% protonated and Copenhagen was 92% protonated
- The pH of the BB Products in complete artificial saliva is approximately 8; the market comparators are lower at 6.7 for General Snus and 7.0 for Copenhagen.
- Degree of protonation or pH does not appear to be affecting the percentage of total nicotine released
- Figures 3 and 4 show the cumulative and percent releases of the BB Products and market comparators.
- Essentially 100% of the nicotine is released from the Long Cut Products after 30 minutes.
- The Pouch Products appear to release nicotine at about the same rate as the market comparator. All of the nicotine is released from the Pouch Products and the market comparator by 60 minutes.
- The Pouch Products released slower than the Long Cut Products (Figure 5)
- The dissolution rate and extent (Table 2) was similar for the Long Cut Products
- The dissolution rate (Table 2) was the same for the Pouch Products and General Snus but General Snus had a lower dissolution extent because it has less nicotine.
- Flavor had no effect on release in either product form

CONCLUSION

- ✓ A significant portion of the nicotine in the BB Products is bioavailable (~80%). All nicotine is released within 60 minutes
- ✓ BB Products release nicotine at rates and to extents similar to currently marketed smokeless products.
- ✓ Release profiles are generally the same within each product form (Long Cut and Pouches)
- ✓ Nicotine release from the Pouches is slower than the Long Cut Flavor had no effect on nicotine release.

Table 1. Nicotine and pH in Artificial Saliva

Product	pH	Total Nicotine (mg/unit)	Free Nicotine (mg/unit)	% of Total Nicotine That Is Protonated	% of Total Nicotine Extracted
Black Buffalo Straight Long Cut	8.2	5.7	3.3	41%	70%
Black Buffalo Mint Long Cut	8.0	5.4	2.7	49%	81%
Black Buffalo Wintergreen Long Cut	8.1	5.7	3.0	48%	78%
Black Buffalo Peach Long Cut	8.2	6.2	3.6	42%	83%
Black Buffalo Blood Orange Long Cut	8.1	6.2	3.3	48%	81%
Black Buffalo Straight Pouches	8.1	7.7	4.0	48%	76%
Black Buffalo Mint Pouches	8.0	7.8	3.7	53%	83%
Black Buffalo Wintergreen Pouches	8.0	7.5	3.6	52%	81%
Copenhagen Long Cut Wintergreen	7.0	7.4	0.6	92%	77%
General Snus Wintergreen Portion White Large	6.7	4.9	0.2	96%	69%

Table 2. Nicotine Dissolution Rate and Nicotine Dissolution Extent

Product – Loose (or “Long Cut”)	Dissolution Rate (%/minute)	Dissolution Extent (mg/unit)
Black Buffalo Straight Long Cut	5	7.5
Black Buffalo Mint Long Cut	5	7.1
Black Buffalo Wintergreen Long Cut	5	7.3
Black Buffalo Peach Long Cut	5	9.2
Black Buffalo Blood Orange Long Cut	5	7.4
Copenhagen Long Cut Wintergreen (market comparator)	5	8.7
Product – Portions (or “Pouches”)		
Black Buffalo Straight Pouches	1.67	8.6
Black Buffalo Mint Pouches	1.67	7.8
Black Buffalo Wintergreen Pouches	1.67	7.8

Figure 3. Nicotine Cumulative and Percent Release Profiles for Long Cut Products

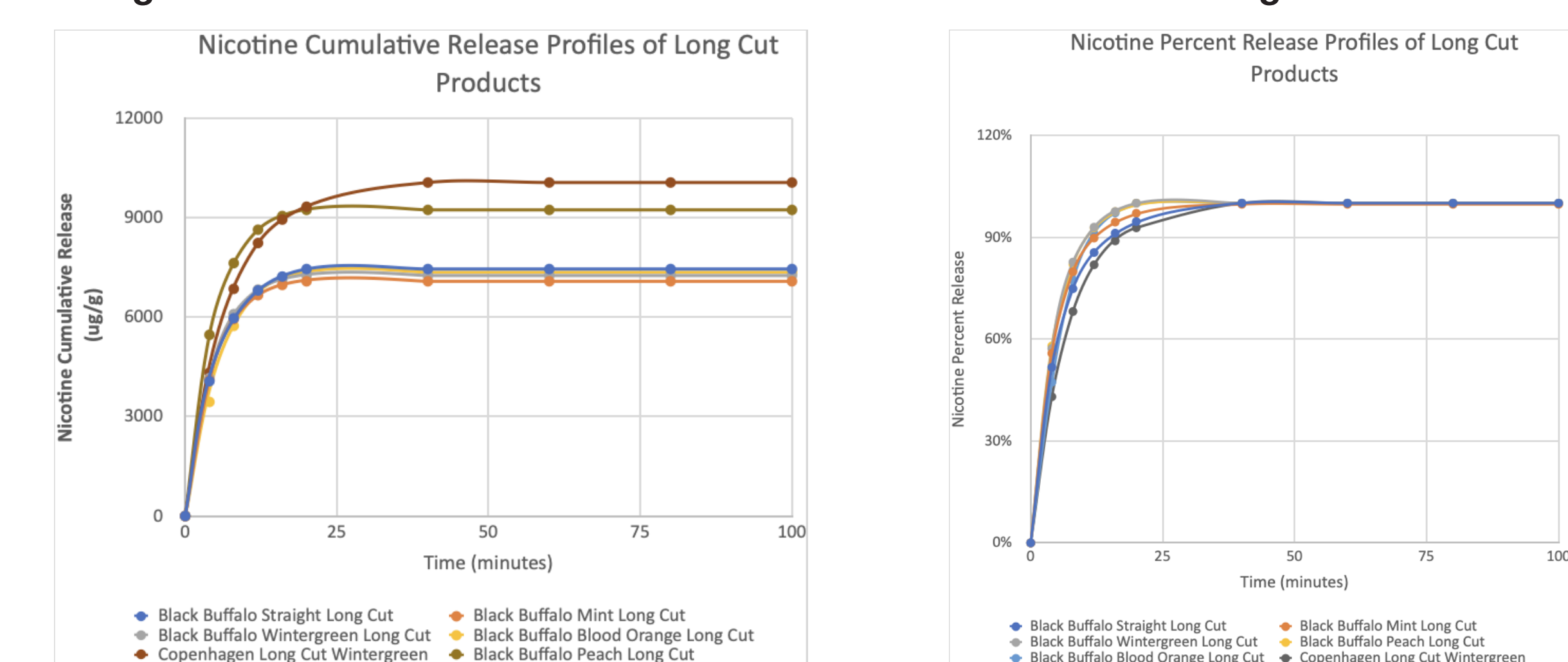


Figure 4. Nicotine Cumulative and Percent Release Profiles for Pouch Products

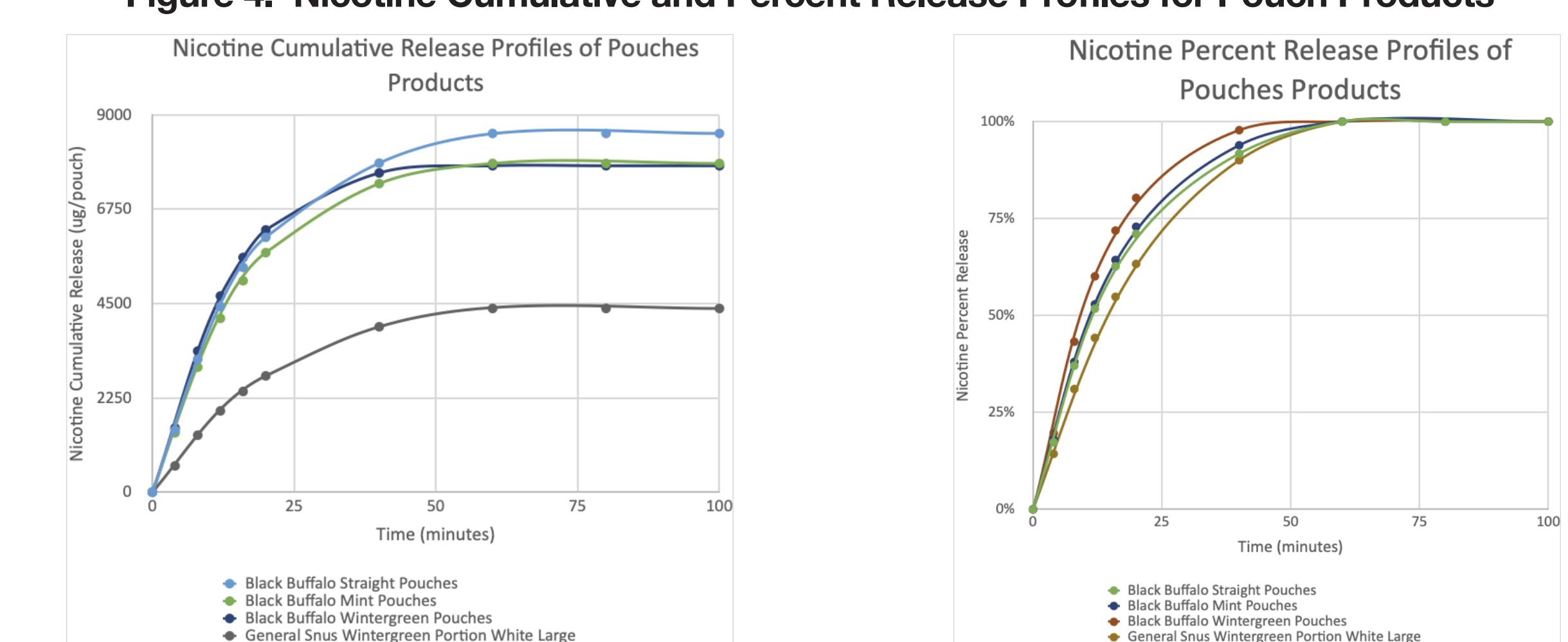
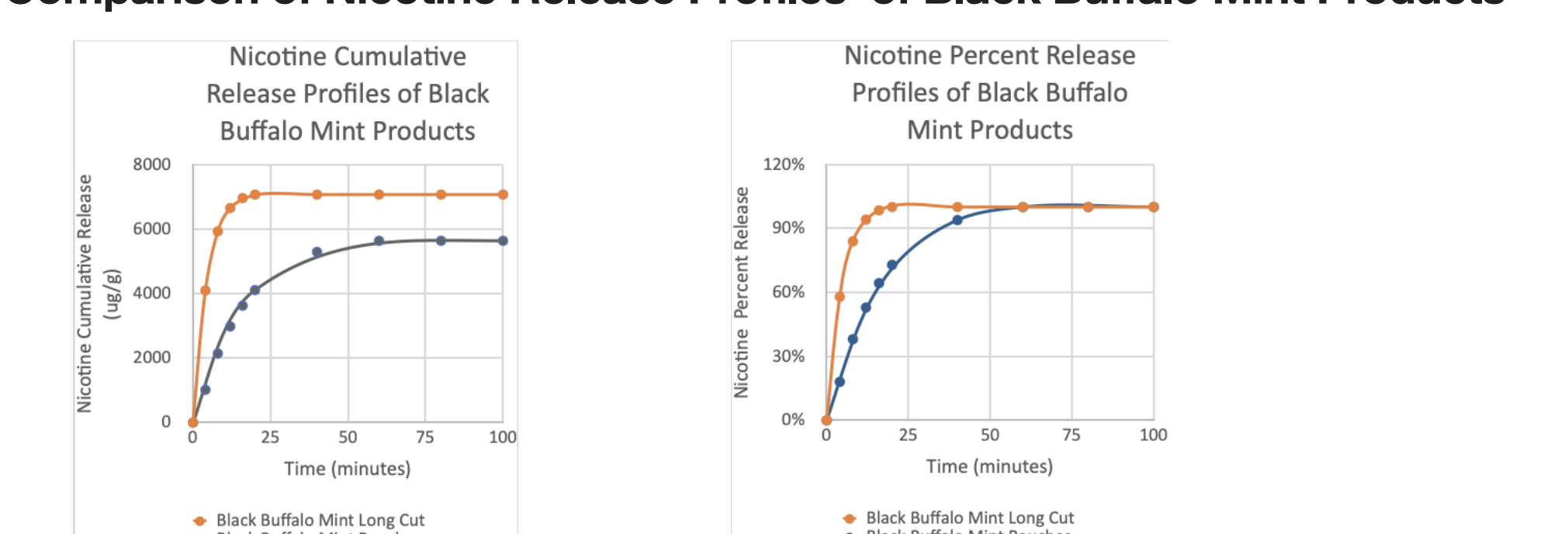


Figure 5. Comparison of Nicotine Release Profiles of Black Buffalo Mint Products



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