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Abstract

The modern oral nicotine product category is quite diverse and includes tobacco-free (plant and fiber-based) pouches, gums, lozenges, pastes, and strips, among others. Products may contain natural or synthetic nicotine, various flavors and sweeteners, and other ingredients unique to the matrix. Consequently, for this multitude of product subtypes, there may be unique rates of nicotine release when consumed, even for products containing similar total nicotine amounts. To our knowledge, a direct comparison of nicotine release profiles for these products has not been published previously. Thus, the aim of this study was to compare the *in vitro* release rates of nicotine from several different product subtypes using mastication and/or dissolution.

A purpose-built chewing apparatus (DRT3 from Erweka) was employed for gums and a USP Type IV dissolution apparatus (CE7Smart from Sotax) for lozenges and pouches, both using artificial saliva as the extraction medium. Nicotine concentration in collected fractions was quantitatively determined by a validated HPLC-UV method.

In general, each product subtype displayed a distinct release profile. For example, the release profiles for nicotine gums tended to plateau after approximately 60 minutes of chewing, whereas modern oral pouches released nicotine at a slower rate and sometimes required over 100 minutes to plateau. Lozenges were tested with 60-minute dissolution conditions but found to release slowly under these conditions, leading to low overall yields.

Samples Tested

Product	Extraction Method	Label Nicotine (mg)
Pouch A	Dissolution (100 min)	4
Pouch B		3
Pouch C		4
Pouch D		4
CORESTA Reference Pouch		7.6
Lozenge A	Dissolution (60 min)	2
Lozenge B		4
Lozenge C		2
Lozenge D		4
Gum A	Mastication (60 min)	4
Gum B		4
Gum C		4

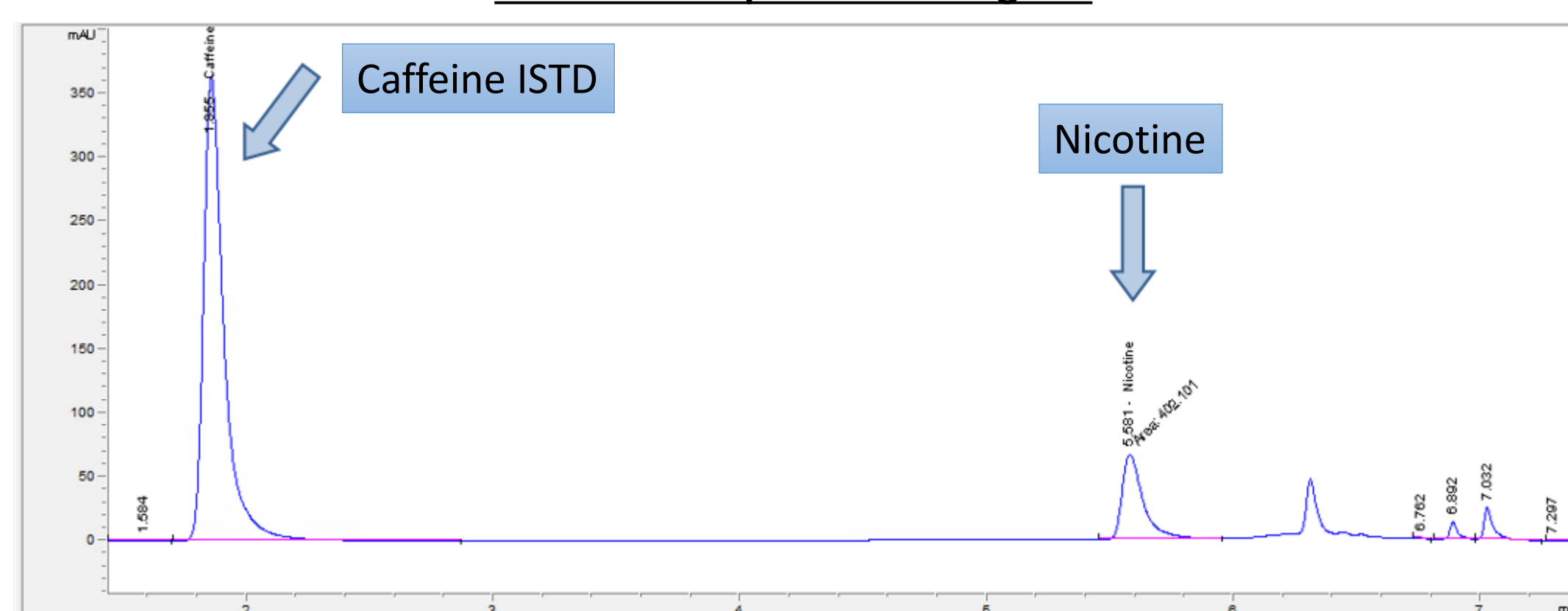
- Products were selected to vary parameters, such as base matrix and nicotine type, expected to impact release characteristics
- The available lozenges provided limited variation for base matrix and nicotine type

Sample Preparation and Analysis by HPLC-UV

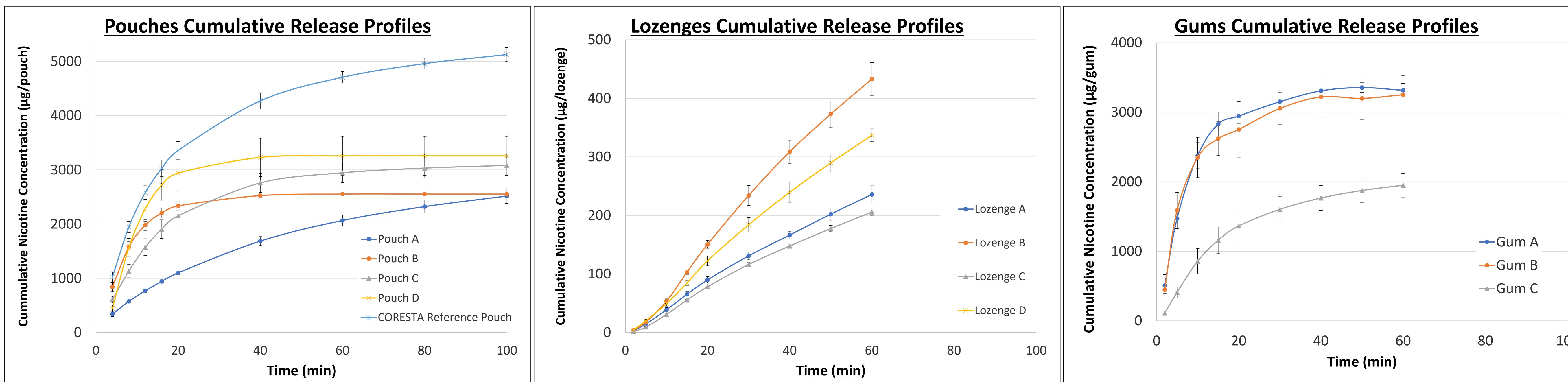
Column: Poroshell HPH-C18 2.1 x 100 mm, 2.7 μ m
Mobile Phase A: 10 mM NH ₄ Ac @ pH 10
Mobile Phase B: Acetonitrile
Detection Wavelength: 254 nm

- Fractions were diluted with ISTD solution prior to analysis by HPLC-UV
- Quantification by internal calibration with caffeine as internal standard
- The linear range of the method was 0.50 – 100 μ g/mL nicotine

Fortified Sample Chromatogram



Nicotine Release Profiles



- Pouches B, C, and D appear to have plateaued within 100 minutes under these experimental conditions
- CRP produced the greatest release level, in agreement with label claims
- Product A displays a slower release and does not plateau within the experimental timeframe
- All lozenges had low release levels (<500 μ g) for these conditions
- 1-hour is insufficient time for full release under Type IV with no agitation
- Offline stirring experiments showed 15 minutes for total dissolution under the highest rpm conditions
- Gums nearly plateau after 60 minutes of chewing
- Products A & B tracked closely, C was an outlier, despite identical label claims
- The gum products appear to plateau sooner than the pouches and lozenges, but the release level at plateau is similar to the pouches (~3000 μ g)

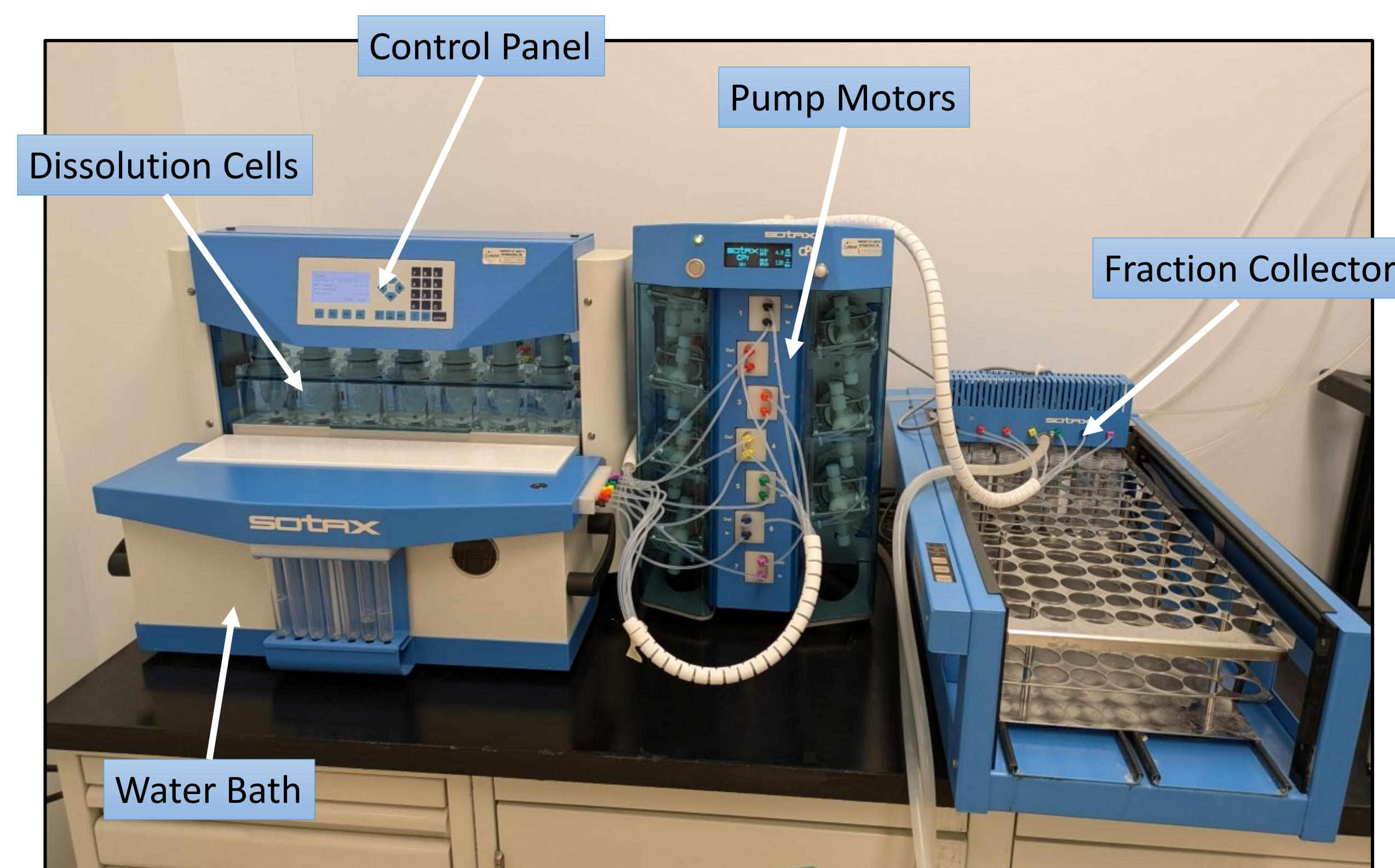
Pouches
Use instruction: Place in mouth, moisten, & hold

Lozenges
Use instruction: Place in mouth, moisten & move around mouth

Gums
Use instruction: Place in mouth & chew

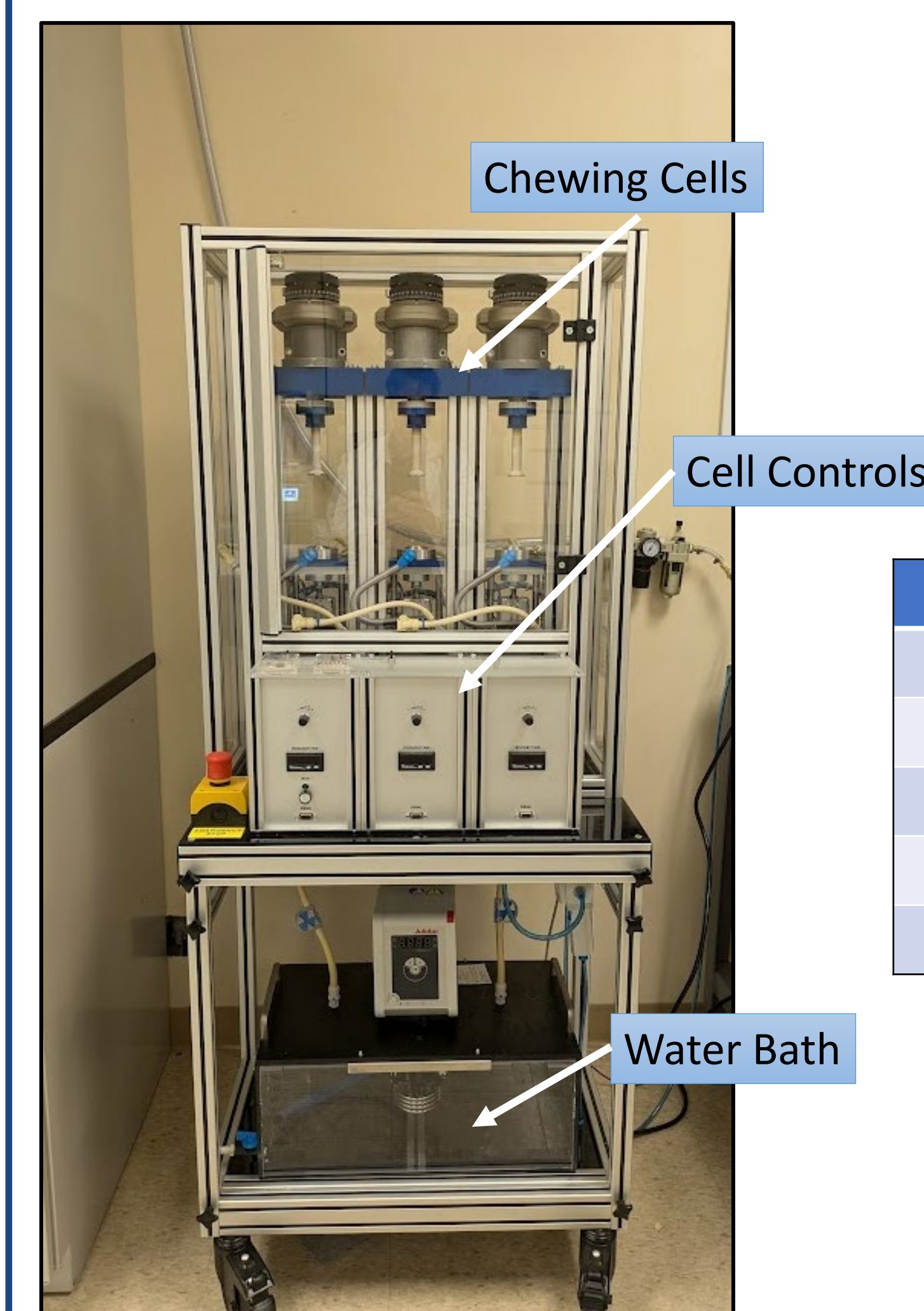
Greater Agitation Required for Nicotine Release

Type IV Dissolution: SOTAX CE7 Smart Flow-Through System



- Samples are installed in a series of six parallel flow cells, plus a reference cell
- Artificial saliva (buffered saltwater recipe) flows through each cell at 4 mL/min
- Saliva is warmed to 37 °C with a water bath
- Type IV dissolution includes no agitation
- All eluent is directed to a series of collection tubes, with programmed fractioning
- For **lozenges**, new fractions began at 2, 5, 10, 15, 20, 30, 40, 50 and 60 minutes
- For **pouches**, new fractions began at 4, 8, 12, 16, 20, 40, 60, 80 and 100 minutes

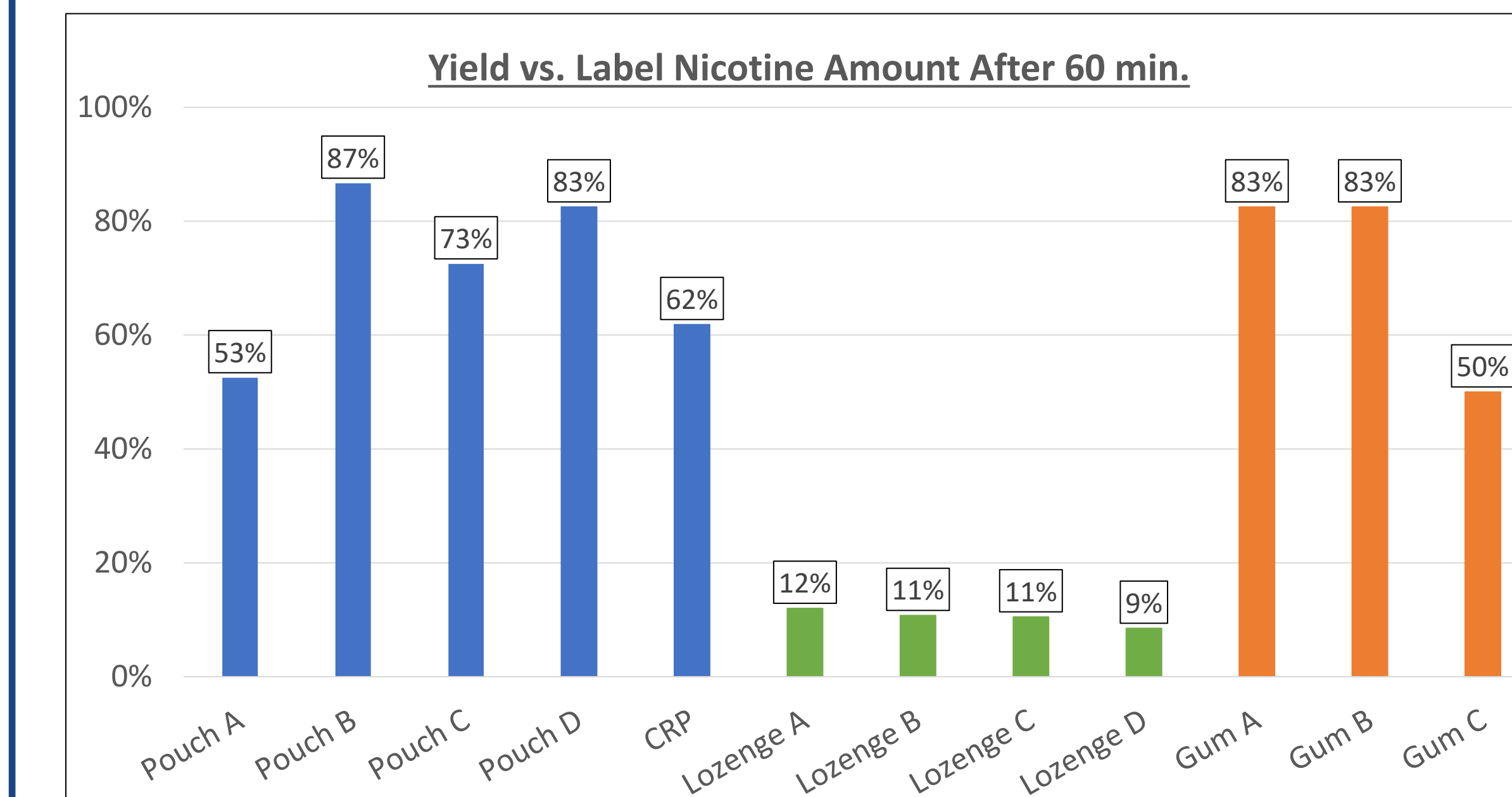
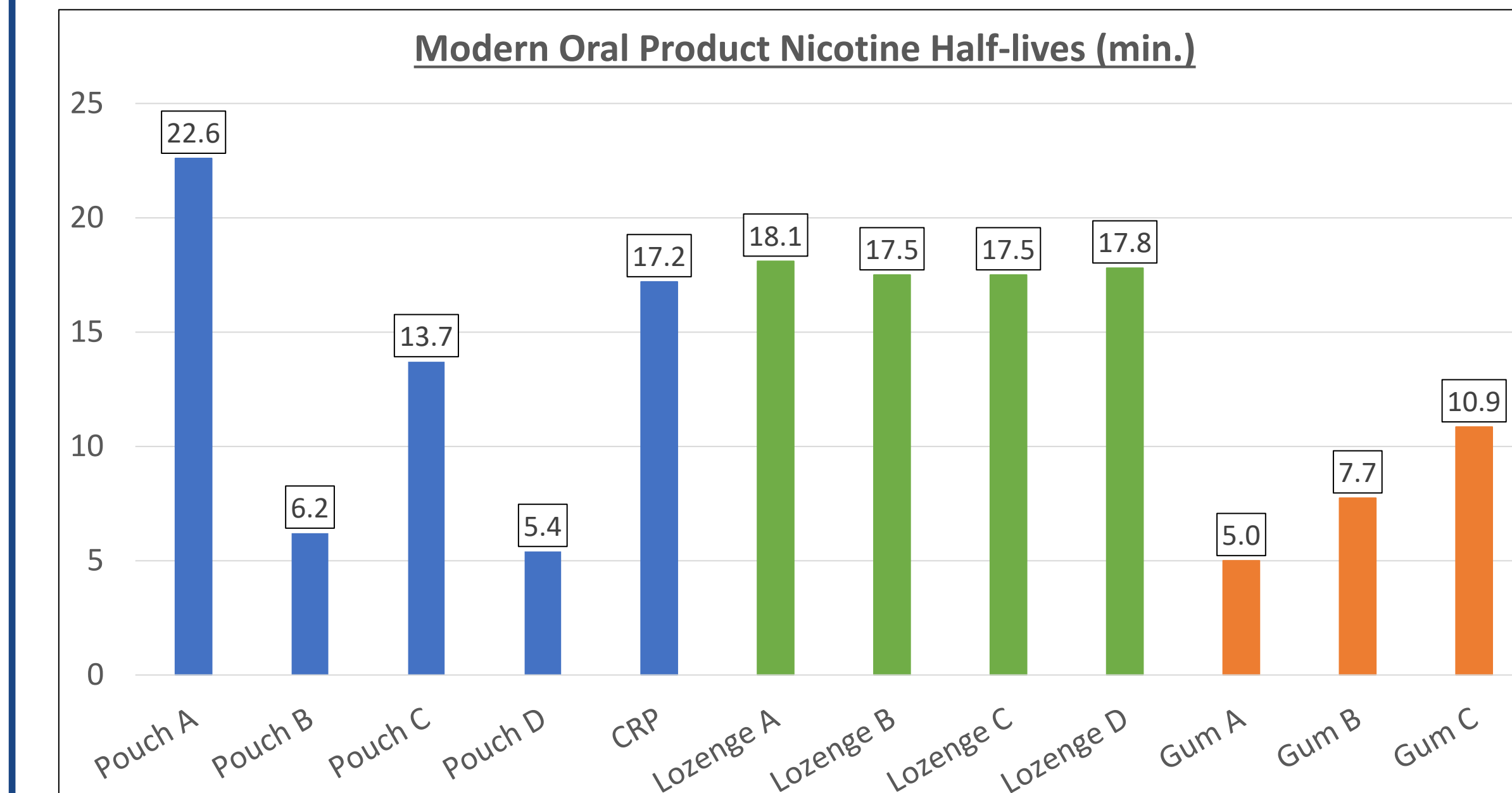
Mastication: Erweka DRT3 Chewing Apparatus



Instrument Conditions	
Jaw Gapping	1 mm
Water Temp	37.5 °C
Twisting angle	20°
Mastication frequency	60 per min.
Saliva cell volume	40 mL

- Samples are installed in each of three chewing cells
- Samples are immersed in a fixed volume of artificial saliva during chewing
- Agitation was programmed to mimic use (high)
- 1 mL aliquots removed and replaced at 2, 5, 10, 15, 20, 30, 40, 50, and 60 minutes

Results and Discussion



- Lozenges produced tightly grouped half-lives, while more variation was observed in gums and pouches
- Pouches showed 50 to 90% of the value after 60 minutes, with minor increases for some after 100 minutes
- Yields were low for all lozenges and release was clearly incomplete, emphasizing the importance of agitation for this product type
- Gums showed 50 to 80% of the value after 60 minutes

Conclusion & Future Work

Using two complementary techniques, nicotine release profiles have been measured for a collection of modern oral products. Significant differences in half-lives were observed for gums and pouches, while lozenges were closely grouped together.

While mastication for 60 minutes proved suitable for gum analysis and dissolution for 100 minutes proved suitable for pouches, nicotine was not fully released from lozenges after the chosen 60-minute period of dissolution, and low overall yields were measured.

To extend our understanding of lozenges' release profiles, Type IV parameters will be further varied, and Type I dissolution will be included in future studies. Release profiles for other modern oral products will be included in comparative studies and reported in a future communication.

The experimental conditions of this study are not intended to represent or be indicative of consumer use conditions of the product.

For more information or to schedule a meeting, please scan the QR code (right) and fill out a request

