Dissolution and Physical Characterization of Oral Nicotine Pouches

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Altria

FAMILY OF COMPANIES

Background and Study Overview

STUDY OF CHEMICAL AND PHYSICAL ANALYSIS
of seven commercially available nicotine pouch products:

on!®

Zyn®

Velo®

Dryft®

Rogue™

Volt™

Loop®

NICOTINE POUCHES are oral tobacco products that DO NOT CONTAIN TOBACCO and are composed of flavorings, sweeteners, and plant-based fibers

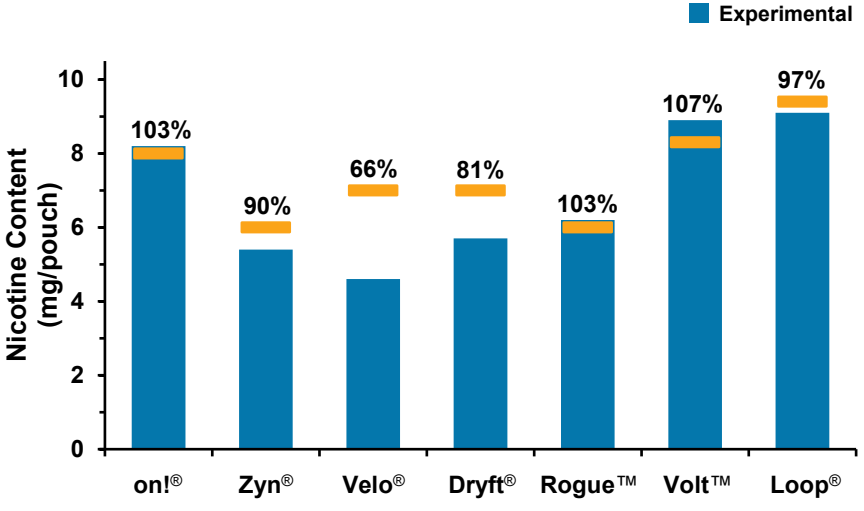
Characterization includes:

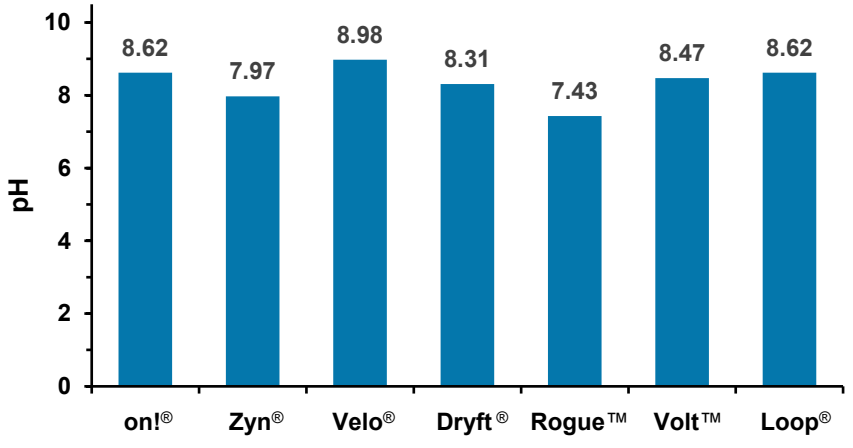
- Nicotine
- pH
- Nicotine dissolution
- Particle size
- Imaging
- Density
- Crystallinity
- Extracted viscosity
- Solubility
- Oven volatiles (OV)

UNDERSCORES THE NEED FOR FURTHER RESEARCH
on relationship between the chemical and physical properties and product performance

Note: Trademarks used for comparison purposes only and ownership in each trademark is retained by its respective owner

Nicotine and pH Determination





Methods:

Nicotine determined using CORESTA CRM No. 62[1]

Calculated content vs. can label

- on!, Rogue, Volt were higher than can label
- Zyn, Velo, Dryft, and Loop were lower than can label

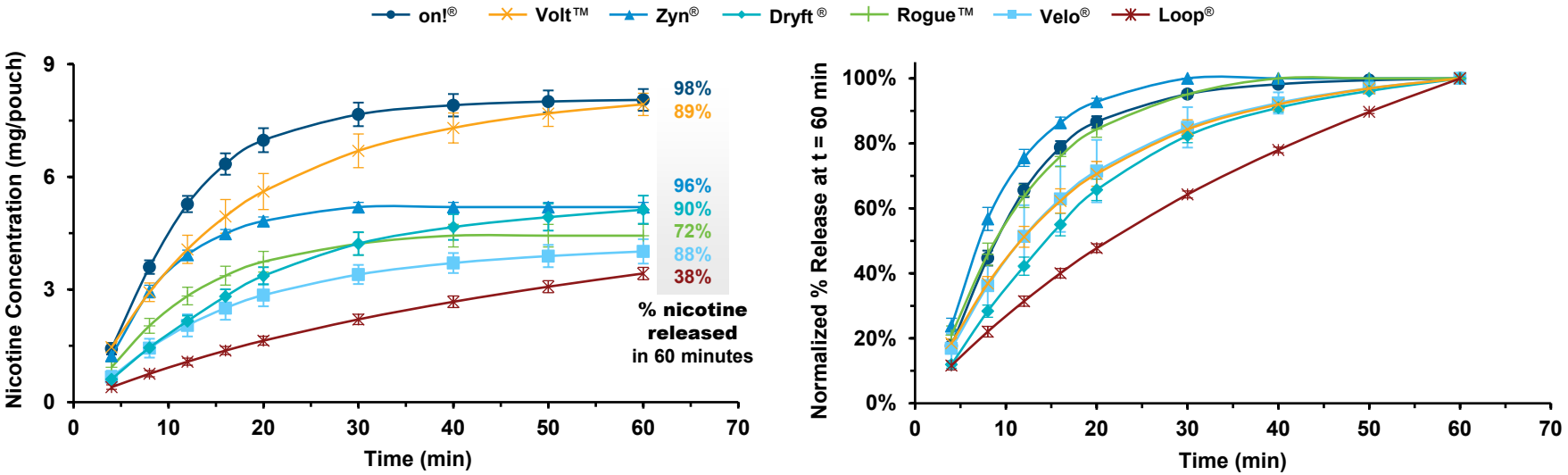
Methods:

pH measured using CDC method[2]

- pH ranged from 7.43-8.98 for all products

1. CORESTA. No. 62: *Determination of Nicotine in Tobacco and Tobacco Products by Gas Chromatographic Analysis*; TTPA-284-2-CRM-62; 2021.
2. Revised Protocol for Analysis of Nicotine, Total Moisture, and pH in Smokeless Tobacco Products. Department of Health and Human Services, C. f. D. a. P., Ed.; Federal Register, 2009; Vol. 74, pp 712-719.

Experimental Dissolution



Carried out using USP-4 flow-through cell apparatus

Volt, Velo, and Dryft have overlapping and equivalent release profiles, **but slower than on!**

Loop is the slowest rate and never reaches a plateau during 60-minute run

Results confirm different performance
between nicotine pouches and their ability to release nicotine

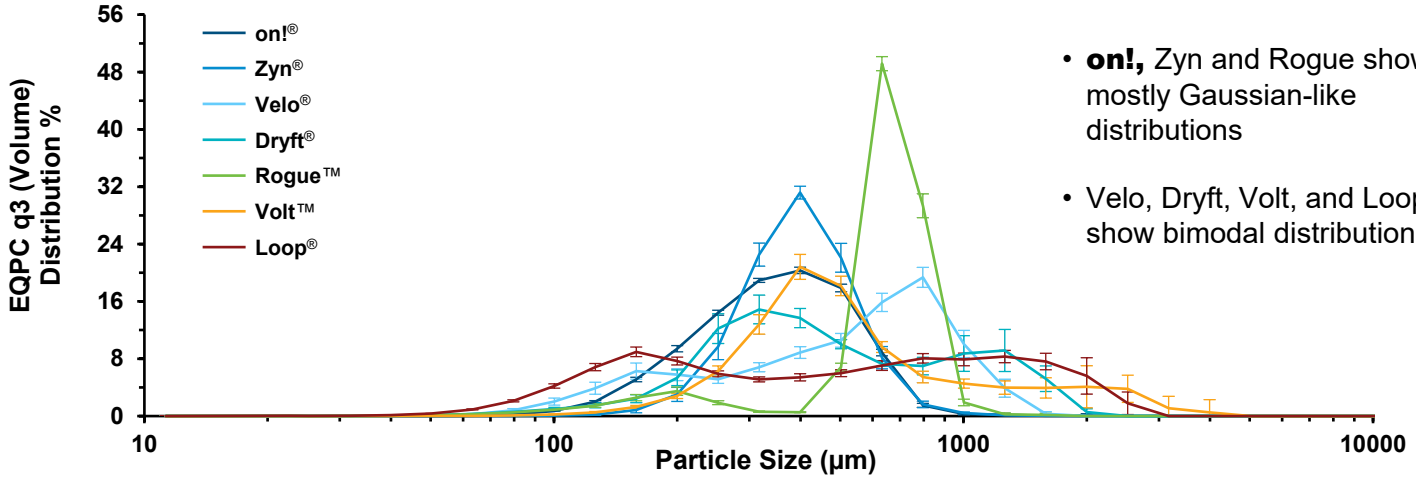
Dissolution Equivalency

Total Nicotine Released at 60 min

	Products	Difference factor (f_1): Calculates the percent difference between two release profile curves at each time point	Similarity factor (f_2): A logarithmic reciprocal square root transformation of the sum of the squared error	Equivalent
on!® vs.	Zyn®	14.3	52.9	Yes
	Rogue™	2.9	81	Yes
	Velo®	14.5	47.3	No
	Dryft®	22.6	38.2	No
	Volt™	14.9	46.6	No
	Loop®	34.4	27.8	No

Miller, J.H.; Danielson,T.; Pithawalla, Y.B.; Brown, A.P.; Wilkinson, C.; Wagner, K.; and Aldeek, F. *J. Chromatogr B*. 2020, 1141, 122012. DOI: 10.1016/j.jchromb.2020.122012.

Particle Size (Dynamic Image Analysis – Volume-Weighted)

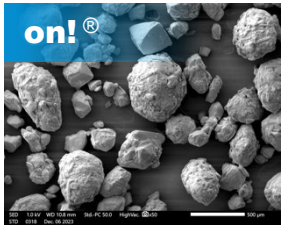


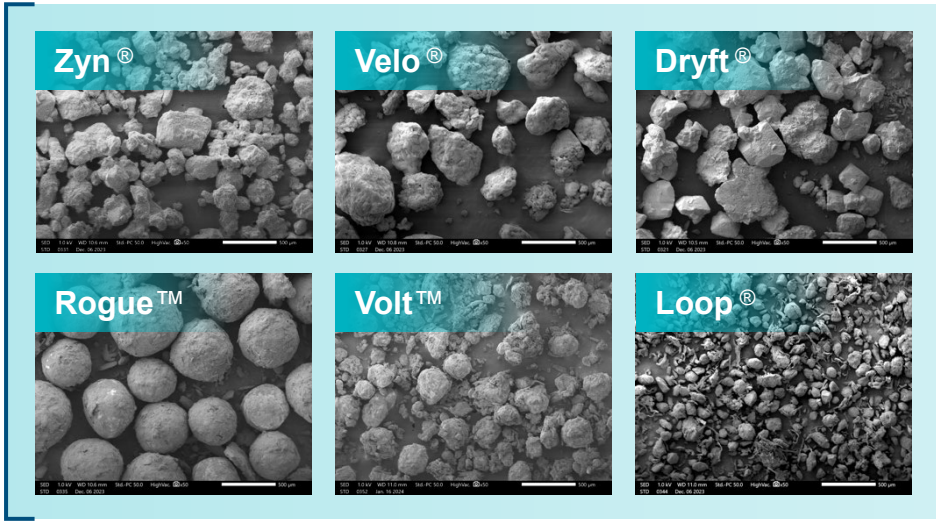
- **on!,** Zyn and Rogue show mostly Gaussian-like distributions
- Velo, Dryft, Volt, and Loop show bimodal distributions

Product	Mean (µm)	d_{10} (µm)	d_{50} (Median, µm)	d_{90} (µm)
on!	334.45	167.20	314.11	515.85
Zyn	367.57	233.18	352.54	511.95
Velo	503.85	143.33	494.91	876.30
Dryft	537.65	191.04	399.79	1121.36
Rogue	562.28	248.44	583.91	753.03
Volt	658.83	242.16	430.56	1543.75
Loop	626.74	108.76	444.42	1468.33

No relationship found between particle size and dissolution across brands of nicotine pouches

Imaging





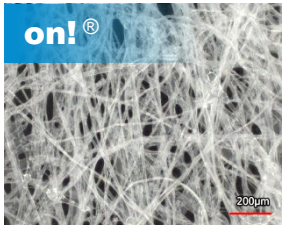
Product	Optical Imaging Sizing (µm)
on!	380.56
Zyn	343.42
Velo	329.56
Dryft	317.98
Rogue	595.47
Volt	296.88
Loop	138.27

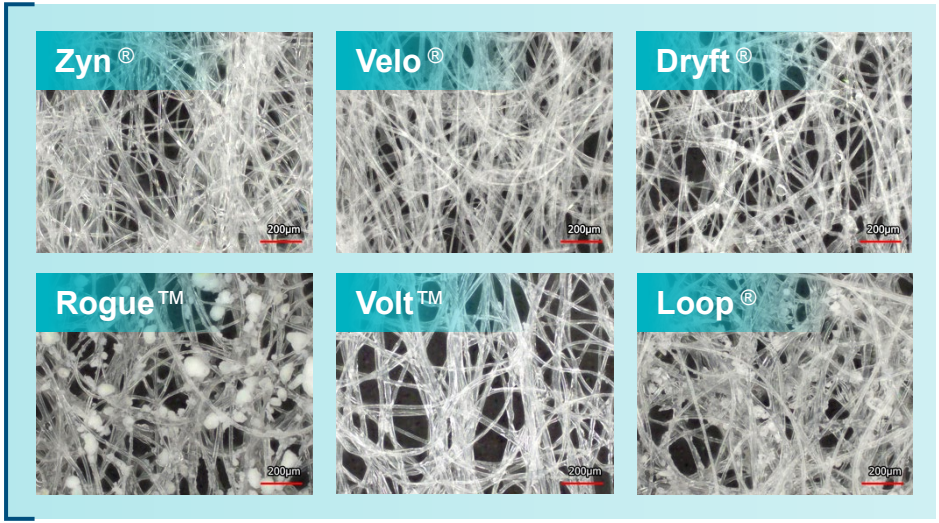
Heterogeneous distribution of particles for most fillers present

(Rogue is exception with spherical homogenous particles)

- Particle size estimated by measuring diameter of 100 particles in one image and averaging diameter
- Loop was dried prior to imaging in a vacuum oven at ambient temperature

Pouch Material Imaging

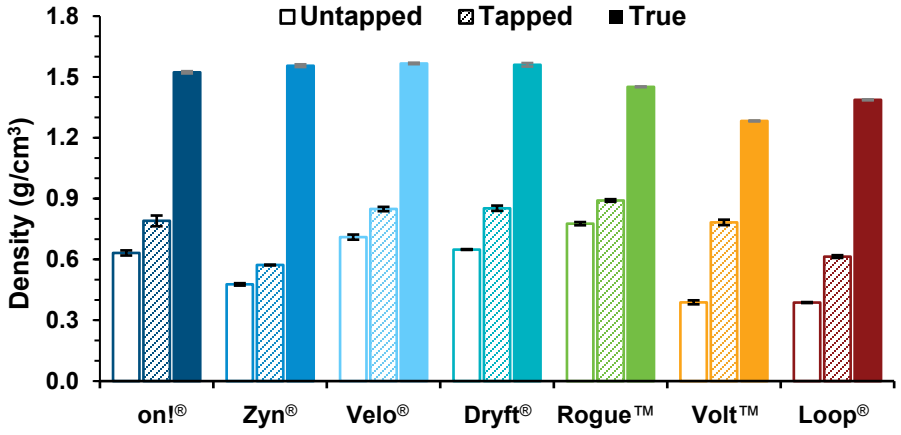




Product	Paper Void Pore Size (µm)
on!	49.219
Zyn	67.951
Velo	49.918
Dryft	52.730
Rogue	73.428
Volt	104.812
Loop	74.777

Average void pore size for all paper was less than d_{10} for corresponding filler

Density and Porosity



Product	Porosity %	Hausner Ratio	Carr's Index
on!	48.11	1.250	20.02
Zyn	63.21	1.200	16.68
Velo	45.84	1.195	16.32
Dryft	45.36	1.314	23.91
Rogue	38.62	1.147	12.85
Volt	39.00	2.015	50.38
Loop	55.74	1.585	36.90

Particle size does not correlate to density values

High and low porosity of Zyn and Rogue indicate large surface and smooth spherical surface of these products, respectively

Flowability ratios:

Hausner Ratio > 1.25:
indicates powder not free flowing

Carr's Index > 25:
indicates poor flowing powder

Porosity

$$P\% = \frac{(\rho_T - \rho_{TB})}{\rho_{TB}} \times 100$$

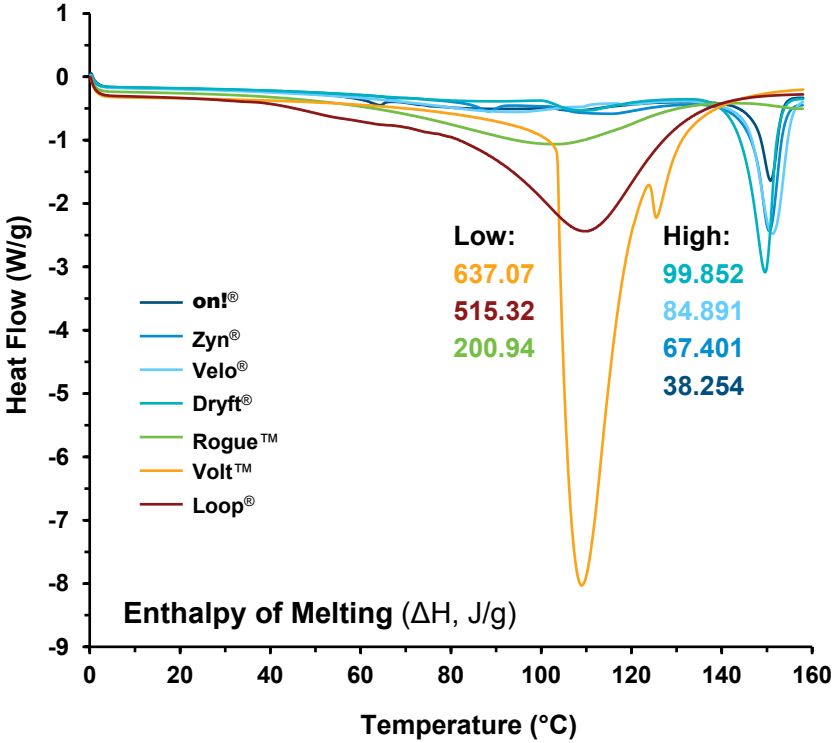
Hausner Ratio

$$H = \frac{\rho_{TB}}{\rho_{UB}}$$

Carr's Index

$$C = \frac{(\rho_{TB} - \rho_{UB})}{\rho_{TB}} \times 100$$

Crystallinity by Differential Scanning Calorimetry (DSC)



TWO GROUPS:

High and Low Melting Point

1 High Melting:

Dryft → Velo → Zyn → **on!**

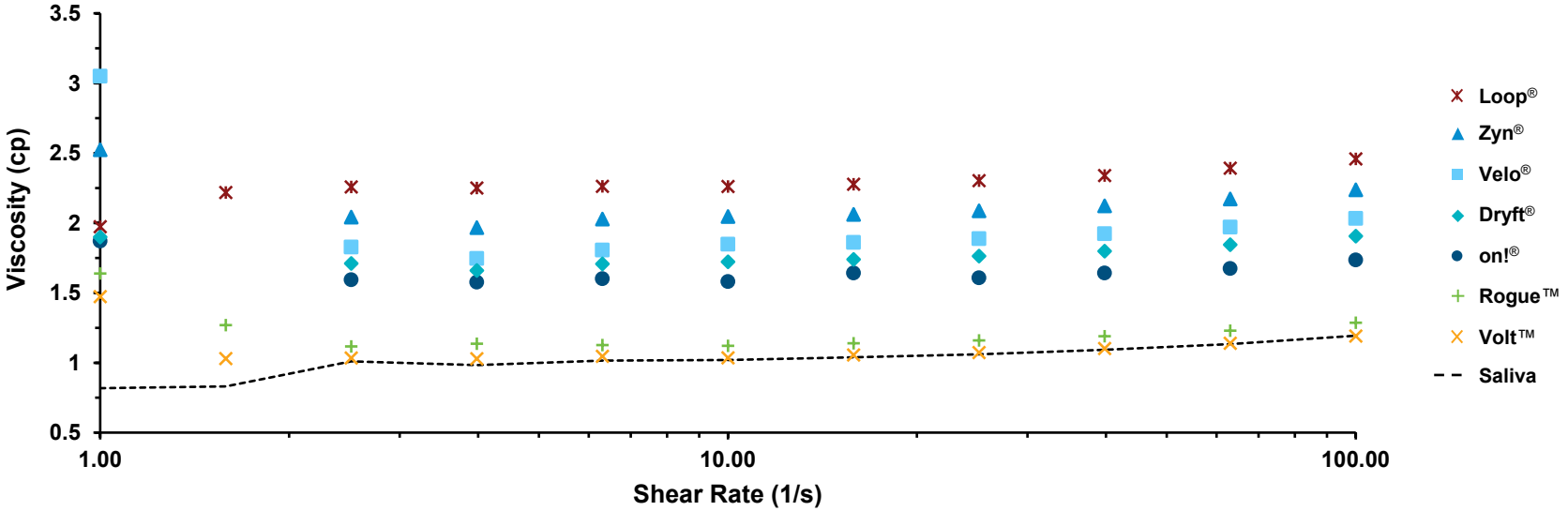
- Melting points around 150°C
- Possess secondary thermal transition at 60-115°C due to water molecules or other additives

2 Low Melting:

Volt → Loop → Rogue

- Melting points around 110°C
- Lower melting leads to lower enthalpy relative to other fillers
- Glass transition temp for Loop due to oil like additive

Viscosity



Viscosity of extracted pouches

in artificial saliva run using concentric cylinder and thermal jacket at ambient temperature

- Artificial saliva shown as reference
- Viscosity of extracted solution can be used to co-relate the property of the solubility of filler

Solubility and Oven Volatiles (OV)

Products	Percent Solubles (%) 1g Filler extracted in 40 mL artificial saliva, filtered, and dried at 120°C for 1 hour	OV (% MC) 2g filler placed in halogen oven at 80°C for 10 min
on!®	66.35 ± 0.15	4.48 ± 0.20
Zyn®	78.26 ± 0.77	3.52 ± 0.08
Velo®	64.41 ± 2.67	6.62 ± 0.23
Dryft®	68.03 ± 0.68	3.71 ± 0.15
Rogue™	41.21 ± 0.35	14.70 ± 0.14
Volt™	59.75 ± 2.54	37.18 ± 1.80
Loop®	N/A	26.64 ± 0.84

High % MC
for **Volt** and **Loop** due to products being wet pouches

Conclusions

Investigated chemical and physical characterization of seven commercially available nicotine pouch products

THIS STUDY

Provides a better understanding of the properties of the studied pouches

and reveals significant differences in their characteristics

- All nicotine pouches are made by different manufacturers using various ingredients and granulation processes, leading to differences in physicochemical properties
- Multiple driving factors do influence the nicotine release and overall performance
- Insights from the study enhance knowledge for developing nicotine pouch products

Any

Questions?