

Chemical characterisation of oral nicotine pouches and comparison to combustible cigarettes

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INTRODUCTION

Nicotine pouches are a recent innovation which contain pharmaceutical-grade, high-purity nicotine combined with a plant-fibre substrate (e.g., wheat or bamboo). Unlike traditional tobacco products, oral nicotine pouches (ONP) do not burn tobacco and do not contain any tobacco leaf. Instead, they deliver nicotine buccally via the gums.

Nicotine pouches have gained popularity among adult

smokers in North America and Europe. However, publicly available scientific data on their harm reduction potential remain limited. In this study, we present chemical characterisation data for four ONP variants (zone[®] nicotine pouches with different flavours and nicotine strengths obtained from the UK market) and provide a toxicological risk assessment of any quantifiable constituents.

ONP were analysed against the GOTHIA TEK[®] analyte list, which includes a range of toxicants such as Tobacco-Specific Nitrosamines (TSNAs), nitrite, NDMA, benzo[a]pyrene, carbonyls, metals, and mycotoxins. From this list, a subset of analytes was compared to levels measured in smoke from the 1R6F reference cigarette, specifically: NNN, NNK, benzo[a]pyrene, acetaldehyde, formaldehyde, crotonaldehyde, cadmium, and arsenic.

METHODS

Test articles

- 1R6F Reference cigarette (University of Kentucky)
- Oral nicotine pouches, zone[®]
 - Flavour 1 (16mg/pouch nicotine)
 - Flavour 2 (16mg/pouch nicotine)
 - Flavour 3 (11mg/pouch nicotine)
 - Flavour 4 (11mg/pouch nicotine)

All products were obtained from the UK market

Test methods

All analyses were conducted using validated methods in an ISO 17025-accredited laboratory.

- 1R6E: ISO 20778:2018¹
- zone[®]
 - Nicotine: CORESTA Recommended Method No. 62
 - TSNAs and Carbonyls: LC-MS/MS method
 - Benzo[a]pyrene: LC-FLD
 - Metals: ICP-MS method

RESULTS

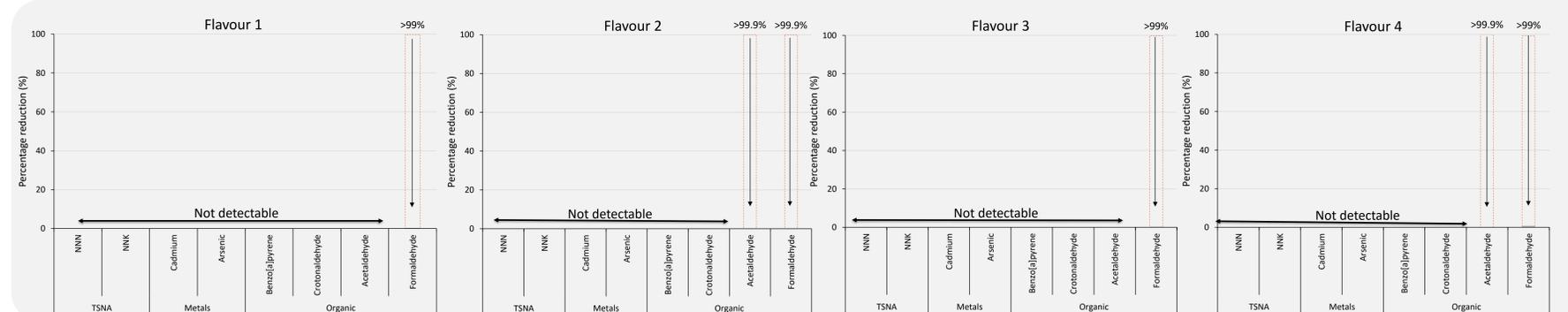


Figure 1: Percentage reduction (orange dashed column) of average toxicants in zone[®] ONP ($\mu\text{g}/\text{pouch}$) compared to the average toxicants in a reference cigarette² ($\mu\text{g}/\text{cig}$) with the overlaid values above indicating the percentage decrease. Measurements were carried out in triplicate except for cadmium and arsenic in cigarettes which were carried out in 4 replicates.

Analyte type	Analyte	Nicotine pouches						Units	Cigarettes		
		Flavour 1	Flavour 2	Flavour 3	Flavour 4	LOQ ¹ equiv.**	Gothiatek limits*		1R6F	LOQ	Units
TSNA	NNN	<LOQ	<LOQ	<LOQ	<LOQ	0.071	N/A	$\mu\text{g}/\text{pouch}$	0.22	0.005	$\mu\text{g}/\text{cig}$
	NNK	<LOQ	<LOQ	<LOQ	<LOQ	0.071	N/A		0.18	0.005	
Metals	Cadmium	<LOQ	<LOQ	<LOQ	<LOQ	0.071	0.36	0.06	0.0005	0.01	
	Arsenic	<LOQ	<LOQ	<LOQ	<LOQ	0.071	0.18	0.01	0.0025		
Organic	Crotonaldehyde	<LOQ	<LOQ	<LOQ	<LOQ	0.143	0.54	35.53	15	1186.33	
	Acetaldehyde	<LOQ	0.16	<LOQ	0.10	0.007	17.85	107.80	9		
	Formaldehyde	0.31	0.08	0.22	0.79	0.057	5.35	107.80	9		
	Benzo[a]pyrene	<LOQ	<LOQ	<LOQ	<LOQ	0.714	0.89	ng/pouch	13.81		4

Key

<LOQ: Below Limit of Quantification

* $\mu\text{g}/\text{g}$ conversion to $\mu\text{g}/\text{pouch}$ was calculated using the average pouch weight of 0.714g (n=12)

**Actual LOQ ($\mu\text{g}/\text{g}$) can be determined from equivalent LOQ ($\mu\text{g}/\text{pouch}$) by multiplying by 1.4x

Toxicological risk assessment

Acetaldehyde (CAS No. 75-07-0) and formaldehyde (CAS No. 50-00-0) were detected at levels above the limit of quantification. Based on an assumed daily use of six pouches³, the maximum estimated exposure to acetaldehyde is 0.96 $\mu\text{g}/\text{day}$ for Flavour 2, while formaldehyde exposure is estimated to reach 4.74 $\mu\text{g}/\text{day}$ for Flavour 4.

Acetaldehyde is a well-characterised metabolite of ethanol following the consumption of alcoholic beverages and is also naturally present in common foods such as fruits, juices, bread, cereals and yoghurt. EFSA established a Tolerable Daily Intake (TDI) of 0.1 mg/kg/day in 2010⁴, corresponding to 6 mg/day (6000 $\mu\text{g}/\text{day}$) for a 60-kg adult⁵, resulting in a Margin of Exposure (MOE) of 6250 for the estimated consumer exposure. For formaldehyde, Health Canada's Guideline Technical Document on drinking water quality derived a TDI of 0.15 mg/kg/day⁶, equivalent to 9 mg/day (9000 $\mu\text{g}/\text{day}$) for a 60-kg adult⁵, yielding an MOE of 1898 for the estimated exposure.

An MOE of 100 or greater is generally considered indicative of low concern for human health⁷. Both compounds exceed this threshold by a substantial margin, supporting the conclusion that the estimated exposures are not expected to pose a concern for consumers health.

CONCLUSIONS

All GOTHIA TEK analytes were below their maximum limits, with only formaldehyde and acetaldehyde detected at quantifiable levels.

When compared to cigarette smoke, these analytes were reduced by approximately 99.2% – 99.9% across all product variants.

A toxicological risk assessment of these two constituents indicated no significant concerns, as potential exposures were below regulatory toxicant limits.

This initial dataset supports the potential role of ONP in tobacco harm reduction by demonstrating marked reduction of toxicants relative to cigarettes.

The potential role for ONP in tobacco harm reduction is further supported by the in vitro investigations of these products that revealed marked reductions in cytotoxicity when compared to cigarette smoke extracts (>200 fold less cytotoxic) and no genotoxicity (under the conditions of Ames and In Vitro Micronucleus tests), see Figure 2. Further investigations can be found in the poster by Stevenson et al., 2026 (Abstract number 3461)

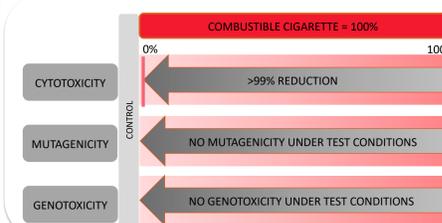


Figure 2: Reductions of biological activity of ONP vs combustible cigarettes. Based on a Zone X #2 product (5.8 mg/pouch) compared to a conventional cigarette TPM. See Yu et al., 2022

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