

Mouth level exposure time on nicotine and TSNA extraction from snus pouches

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INTRODUCTION

Measuring the amount of constituents extracted by snus consumers during use is a valuable step in estimating their exposure to tobacco constituents. A factor potentially influencing the extent of exposure is the length of time that individual consumers keep snus pouches in their mouths during use. A recent survey of snus use in Sweden established that, on average, use of pouched snus extends from approximately 30 minutes to just less than 2 hours¹. The objective of this study therefore was to quantify the importance of use duration on constituent transfer from pouched snus to the consumer over this timescale.

METHODS

User Trial

30 volunteer pouched snus users gave informed consent and took part in a central location study split between Stockholm and Lund, Sweden. The following recruitment criteria were employed:

- Males, aged 19 – 65 years old
- Users with a minimum of 6 months snus use
- Daily users of brown, 1g pouched snus products
- Users of a minimum of 8 pouches per day, for one hour or more per use
- Users who place the pouch in their mouth, under their upper lip
- Users with no dislike for the Lucky Strike brand

Each volunteer used a 1g pouch of the commercial Lucky Strike Original snus product, for ten different duration periods (from 5 to 120 minutes), randomly ordered over 3 sessions. Throughout their sessions, volunteers were required not to consume food, beverages or tobacco products, other than as directed. Drinking water was allowed during breaks of 15-30 minutes provided between each pouch use.

After use each used pouch was collected in an individual glass vial, and a corresponding unused pouch taken from the same tin of snus was collected in a second glass vial. At the end of each session, all portions were stored frozen (-20°C) at the study site prior to shipping to the BAT Analytical Laboratories in the UK in cool boxes containing ice packs. On arrival at the laboratories all portions were stored in a freezer (-20°C) for a minimum of 24 hours and a maximum of 11 weeks prior to analysis.

Sample Analysis

Each used and unused pouch was thawed at room temperature for 1 hour, prior to extraction *in situ* with methanol (20mL). An aliquot of the extract was analysed for nicotine, and a further aliquot was analysed for four tobacco-specific nitrosamines (TSNAs) NAB, NAT, NNK and NNN, using standard analytical methods. This multi-constituent method employing methanol extraction has been described in a previous presentation².

Calculation of Exposure

From the wet-weight basis, per-portion analytical data, values for amount extracted and for percentage transfer of each constituent to the volunteer were calculated for each pair (used and unused) of samples using the equations below:

Amount extracted = Quantity in unused pouch – Quantity in used pouch

Transfer (%) = 100 * (Amount extracted / Quantity in unused pouch)

In the case of TSNAs, the values for the four individual TSNAs were summed, resulting in a value for total TSNAs.

RESULTS

After removal of identified outliers, mean values were calculated for the amount extracted and percentage transfer of nicotine and TSNAs for all participants at each time point. The values are presented with standard deviations in Table 1.

REFERENCES

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Duration of Use (mins)	Mean Amount of Nicotine Extracted \pm SD (mg/pouch)	Mean Nicotine Transfer \pm SD (%)	Number of participants	Mean Amount of TSNA Extracted \pm SD (ng/pouch)	Mean TSNA Transfer \pm SD (%)	Number of participants
5	0.54 \pm 0.67	4.8 \pm 5.7	30	82 \pm 79	5.8 \pm 5.6	30
10	0.83 \pm 0.90	7.3 \pm 7.2	30	100 \pm 57	7.3 \pm 3.9	28
15	1.23 \pm 1.24	10.6 \pm 9.6	30	136 \pm 93	9.8 \pm 6.5	30
20	1.51 \pm 0.93	13.7 \pm 8.1	30	188 \pm 105	13.9 \pm 7.3	30
30	1.98 \pm 0.91	18.1 \pm 7.9	30	249 \pm 94	18.3 \pm 6.9	30
45	2.74 \pm 1.33	24.6 \pm 10.3	30	298 \pm 99	22.1 \pm 6.8	28
60	3.44 \pm 1.11	31.2 \pm 9.2	30	400 \pm 104	29.7 \pm 7.7	30
75	4.07 \pm 1.56	36.9 \pm 11.8	29	485 \pm 141	35.4 \pm 9.0	29
90	4.62 \pm 1.10	42.2 \pm 8.4	30	533 \pm 102	39.6 \pm 6.4	28
120	5.49 \pm 1.11	50.7 \pm 8.3	30	660 \pm 104	49.3 \pm 7.8	29

Table 1: Means and standard deviations for amount of nicotine and TSNA extracted and percentage transfer after each usage duration

Table 1 shows that transfer of nicotine and TSNAs was found to increase with increasing usage duration, with a mean transfer of 5-6% after 5 minutes use, increasing to around 50% after 120 minutes use. Similar mean percentage extractions were observed for nicotine and TSNAs at a given usage duration, regardless of the substantial difference in magnitudes at which these constituents are present in the product. Regression analysis confirmed a statistically significant ($p < 0.001$) relationship between percentage transfer of nicotine and TSNAs, and usage duration.

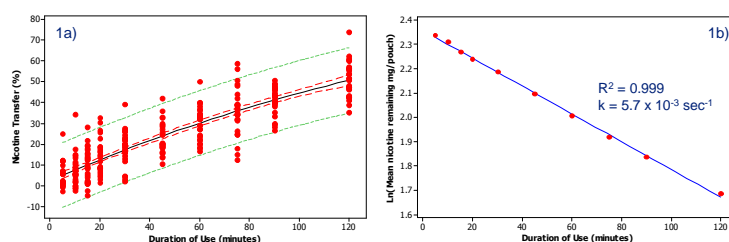


Figure 1: a) Fitted line plot of individual values for % nicotine transfer after each usage duration and b) 1st order kinetic plot of mean nicotine remaining per pouch.

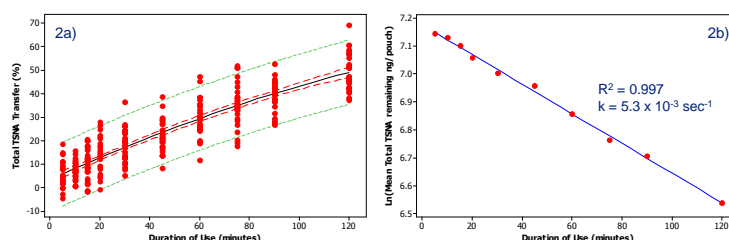


Figure 2: a) Fitted line plot of individual values for % total TSNA transfer after each usage duration and b) 1st order kinetic plot of mean total TSNA remaining per pouch.

Figures 1a and 2a show fitted line plots of nicotine and TSNA transfer, respectively, with the red broken lines corresponding to 95% confidence intervals and the green broken lines corresponding to 95% prediction intervals.

Figures 1b and 2b show that a first order kinetic analysis fits the experimental data very well. Constituent transfer is also consistent with concentration-gradient driven Fickian diffusional processes if the concentrations of nicotine and TSNA in saliva during use are low.

The findings are consistent with those from recent pharmacokinetic studies^{3,4} which showed that t_{max} for peak plasma nicotine concentration appears to be linked to duration of snus use.

CONCLUSION

Exposure of snus users to tobacco constituents such as nicotine and TSNAs increases significantly with the duration of use; the extraction process is consistent with first order kinetics.

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