

# Measuring of two Tobacco-specific Nitrosamines in Indoor air was Developed and Validated

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## Brief Report

The researchers devised and validated a sensitive and accurate method for measuring 1-Demethyl-1-nitrosanicotine (NNN) and 4-(methylnitrosamino)-1-(3-Pyridyl)-1-butanone (NNK) in indoor air. To achieve this, a unique method for collecting two tobacco-specific nitrosamines was used, which included the use of silica sorbent cartridges, streamlined sample preparation, and isotope dilution liquid chromatography/electrospray ionisation tandem mass spectrometry. When compared to approaches that used conventional trapping, this procedure resulted in a significant increase in sensitivity and sample throughput. A matrix-based approach with an accuracy profile procedure was used for validation. Background air samples, environmental aerosols of a heat-not-burn tobacco product (Tobacco Heating System [THS] 2.2, commercialised under the brand IQOS®), a rechargeable electronic cigarette (Solaris®), and the environmental tobacco smoke (ETS) of a conventional cigarette (Marlboro Gold®) were all used as matrices for the study.

The recovery, sensitivity, and precision of the approach were all excellent. For NNN and NNK, the method's detection limits were 0.0108 ng/m<sup>3</sup> and 0.0136 ng/m<sup>3</sup>, respectively. The instrument's calibration range was 0.2–60 ng/mL. The method's determined lower working range limit (LWRL) for NNN was 0.126 ng/m<sup>3</sup>, while NNK's LWRL was 0.195 ng/m<sup>3</sup>. The technique was used to assess surrogate ambient aerosols produced by smoking machines. Because the retention of NNN and NNK in the bodies of consumers is not taken into consideration, this model produces a considerable overestimation of the likely influence of THS 2.2 and e-cigarettes on indoor air. As a result, the given values do not reflect a real-life situation. THS 2.2 had 0.0830–0.0153 ng/m<sup>3</sup> of NNN and 0.0653–0.0138 ng/m<sup>3</sup> of NNK in the surrogate environmental aerosols, 0.0561–0.0296 ng/m<sup>3</sup> of NNN in e-cigarettes, and 0.816–0.109 ng/m<sup>3</sup> of NNN and 4.13–1.04 ng/m<sup>3</sup> NNK in cigarettes. These values correspond to 10% of the measured ETS concentration for NNN in THS 2.2 environmental aerosols and 7% for e-cigarette aerosols. For NNK, the THS 2.2 value for the environmental aerosol was 2% of the ETS value.

Tobacco-specific nitrosamines (TSNA) are carcinogens that have been linked to tobacco, tobacco smoke, and nicotine-containing goods. N-nitrosornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone; nicotine-derived nitrosamine ketone (NNK) were both shown to cause lung cancer in mice in 1964 and 1980, respectively. TSNA can be found in trace amounts in freshly harvested tobacco, but their concentration varies depending on the type of tobacco and fertilisers used throughout the growing process. Nicotine nitrosation is the primary source of NNN and NNK, while nornicotine nitrosation can also produce NNN. This happens most often when tobacco and tobacco

products are processed, cured, and stored. NNK and NNN are partially derived from the distillation of these nitrosamines, which are pre-formed in the tobacco, and NNK is also a result of thermal release of the matrix-bound form, while another fraction is pyrosynthesized by nitrosation of the respective alkaloid precursors, possibly with nitrogen oxides derived from the nitrate, which is present in high concentrations in some tobacco types. Sidestream smoke contains NNK and NNN, and their yields are similar to or two to five times higher than those found in mainstream smoking.

The researchers devised and verified a sensitive and accurate method for analysing two TSNA (NNN and NNK) in indoor air. A unique strategy for the collection employing silica sorbent cartridges with simplified posterior sample preparation was used to reduce the steps during sample preparation as well as the efficient concentration of the target compounds before analysis. After that, the extracts were examined by isotope dilution LC-MS/MS. When compared to the traditional methods of trapping on Cambridge filters, our procedure enhanced sample preparation recoveries. Furthermore, compared to previous methodologies on TSNA studies in air, the LOD and LLOQ were reduced by one to two orders of magnitude.

The accuracy profile process allowed the method's performance to be evaluated as a function of the matrices. In the matrices under examination, the method's working ranges allowed quantification of the target analytes with a precision of 25%. The method's fitness for purpose for prospective comparative analyses of the ambient aerosol of THS 2.2 and e-cigarettes, as well as the ETS of cigarettes, was established by the validation results [1-5].

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