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Methods of Environmental Tobacco Determination by Gas Chromatography

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Abstract

Tobacco smoke is a known carcinogen and otherwise dangerous mixture of compounds. To determine the amount of tobacco smoke actually present in air samples, a quantifiable method must be used. A review of gas chromatographic procedures to analyze for concentrations of commonly used marker compounds (nicotine and 3-ethenylpyridine) is made. Methods of sample adsorption, sample desorption, and injection are discussed. The commonly used flame ionization detectors, nitrogen-phosphorus detectors, and mass analyzers are compared by detection limit between sources to determine the best method of analyzing concentration of the markers. Notable examples of indoor and outdoor cigarette smoke are explored and discussed in regard to the possible effects of ultraviolet radiation and time of day on the samples.

Second hand smoke has become an important political and health issue in the growing population of the Earth. Tobacco smoke is a known carcinogen, and it produces carbon dioxide as a byproduct, which may contribute to the greenhouse effect. While some aspects of secondary inhalation of tobacco smoke, also known as second hand smoke, are still under much debate, there is still an unnaturally large quantity of it in the atmosphere which is available to be introduced to other systems. Therefore, it is important to quantify the effect of combusted tobacco on the environment to provide a framework for qualitative work done on the subject. This is not a simple task. While it may be simple to quantify the constituents of a single cigar smoked, the environmental differences in and out of doors as well as the inconsistent local saturation of the chemicals produces a span of values which is difficult to truly ascertain. While some modernized nations may be making headway in curtailing smoking within their borders, smoking is a much more significant issue in third world countries. To attempt to produce quantifiable results of the environmental tobacco derivative levels, a number of methods have been used. The most common and successful method is gas chromatography, sometimes in conjunction with spectroscopy.

In order to describe the tobacco smoke in atmospheric conditions, the nature of the smoke must be determined. Generally speaking, there are two chemical markers which are most commonly used to denote tobacco presence, nicotine and 3-ethenylpyridine.^{1, 2, 3} Nicotine is the better known component of tobacco (Fig. 1). This nitrogenous compound is produced by some plants as a defense mechanism against insects. In mammals, it is known to have a psychoactive effect by acting as a stimulant. Rather than being a primary component of

¹ Bertoni, G., V. Di Palo, et al. (1996). "Fast Determination of Nicotine and 3-Ethenylpyridine in Indoor Environments." *Chromatographia* **43**(5/6): 296-300.

² Koszowski, B., M. L. Goniewicz, et al. (2009). "Simultaneous determination of nicotine and 3-vinylpyridine in single cigarette tobacco smoke and in indoor air using direct extraction to solid phase." *International Journal of Environmental Analytical Chemistry* **89**(2): 105-117.

³ Kuusimäki, L., K. Peltonen, et al. (2006). "A modified method for diffusive monitoring of 3-ethenylpyridine as a specific marker of environmental tobacco smoke." *Atmospheric Environment* **40**(16): 2882-2892.

tobacco, 3-ethenylpyridine (3EP) is a byproduct the smoldering of the conical ember of a cigarette or other similar product, known as sidestream smoke (Fig. 2).² It has been suggested that 3EP is a product of nicotine pyrolysis. The mechanism for this reaction is not known. Generally speaking, 3EP is a better determinant of tobacco smoke than nicotine. This is because nicotine is prone to undergo photodegradation in the presence of ultraviolet radiation, but 3EP has a significantly greater half-life.¹ Both species produce similar detection limits, as low as 0.06µg per cigarette analyzed.² For analysis of long term tobacco effects, 3EP is the better choice as an analyte since it produces similar results yet lasts longer in the environment.

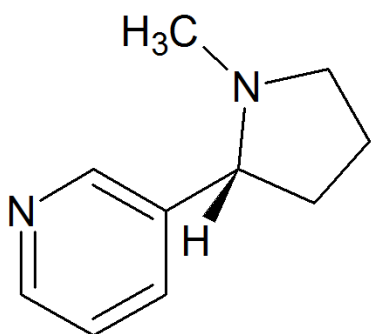


Figure 1: Nicotine structure

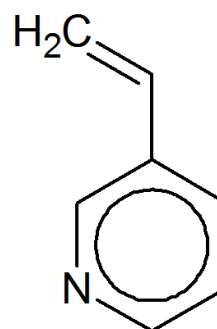


Figure 2: 3-Ethenylpyridine structure

Smoke is a complex mixture of chemicals, and only two are studied in this review because the concentration of one will have a linear relationship to the concentration of the entire mixture under the same conditions. Tobacco smoke can be categorized into two different phases. The particulate phase, consisting primarily of soot, is analyzed by absorbance of total fraction of suspended matter, and the gaseous phase is analyzed for the specific markers such as nicotine and 3EP.³ Nicotine is present in both the gaseous and the particulate phase, albeit in different quantities. This difference arises from the susceptibility of the molecule to degradation in ultraviolet radiation (Fig. 3). As the figure indicates, when nicotine is exposed to UV light the concentration of nicotine in the gaseous phase decreases and the concentration of nicotine in

the particulate phase increases. At the same time, the concentration of 3EP remains relatively steady. Occasionally the line between particulate and gaseous phase blurs, in the case of nicotine dust.⁴ Nicotine dust is the settled combination of the gaseous and particulate phases. This exhibits unique properties that are beyond the scope of this study.

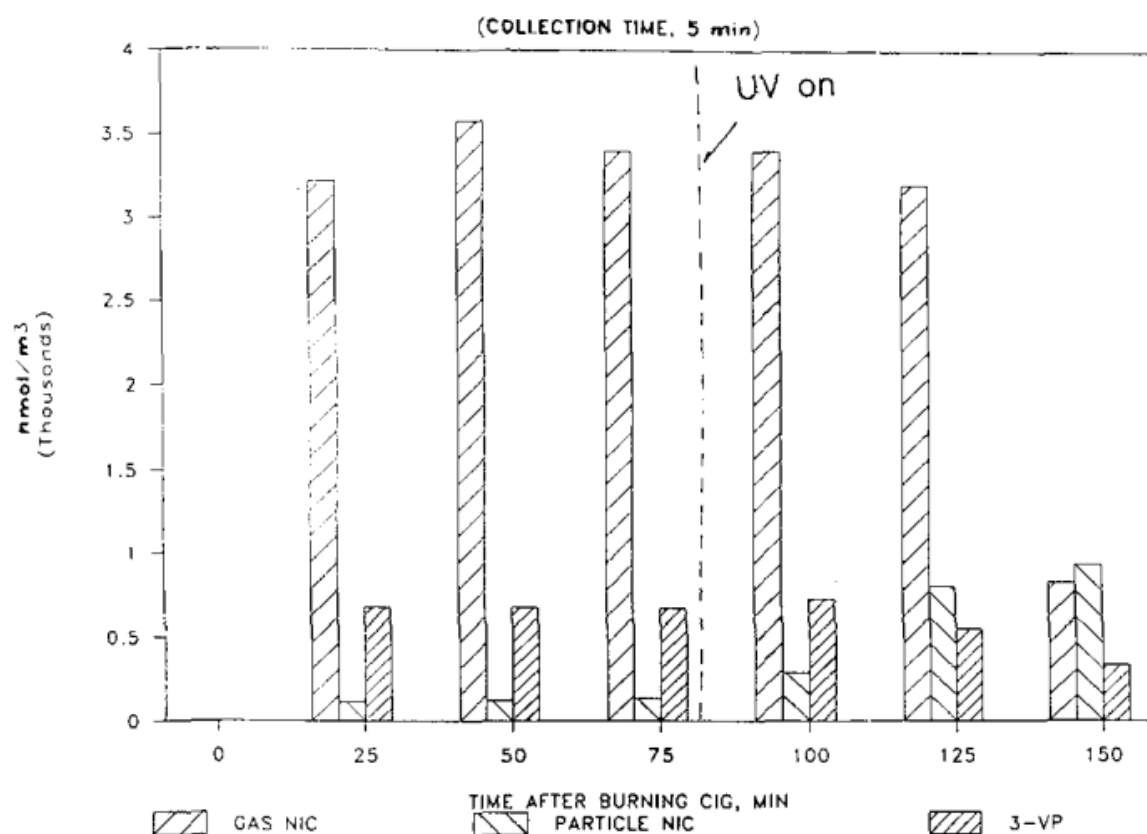


Figure 3: UV light effects on concentrations of nicotine in the gaseous phase and particulate phase and 3EP (Tang et al)

Since UV radiation levels vary based on location type, it is also important to separate the different environments being studied, indoor and outdoor air. Indoors, the environment is further

⁴ Kim, S., T. Aung, et al. (2008). "Measurement of nicotine in household dust." *Environmental Research* 108(3): 289-293.

divided into two groups for study, those exposed to smokers and those exposed to no smoke.⁵ The smokeless indoor environments provide a baseline control group to reference the difference in air quality. Indoor areas which have smoke exposure can vary from very little smoke in the case of an apartment where the neighbor smokes inside but the tenant of the apartment studied does not, to areas with heavy smoker traffic such as designated smoking areas in offices and restaurants. It is expected that higher trafficked areas will have a higher concentration of nicotine and 3EP than those that are not frequented as much by smokers. Outdoors, the air sampling is defined by those both near highly trafficked areas by smokers such as designated smoking areas and around outdoor ashtrays, and those with little to no traffic such as children's playgrounds and roadways.⁵

Most modern analysis of gaseous phase nicotine levels, using either the nicotine or the 3EP as a marker, is done by gas chromatography.⁶ Other techniques can also be used, such as liquid chromatography, but they are used to a lesser extent. Gas chromatography is a technique which allows for the separation of a mixture into its base components, thus making it simple to discern and quantify the individual concentration of each partition in the sample. The sample is pushed through a column of exposed media by an inert carrier gas using either an isothermal temperature or a temperature ramp. The partitions separate by affinity for the exposed media based on polarity.

Modern tobacco smoke analysis occurs either by headspace or adsorptive methods.^{7, 8} Headspace analysis entails the sampling and determination of volatile gas in a chamber with a

⁵ Bertoni, G., C. Ciuchini, et al. (2004). "Long-term diffusive samplers for the indoor air quality evaluation." *Annali Di Chimica* **94**(9-10): 637-646.

⁶ Pandey, S. K. and K.-H. Kim (2010). "A review of environmental tobacco smoke and its determination in air." *TrAC Trends in Analytical Chemistry* **29**(8): 804-819.

⁷ Grob, K. (2001). *Split and Splitless Injection for Quantitative Gas Chromatography: Concepts, Processes, Practical Guidelines, Sources of Error*. 4th ed. Wiley-Vch. Weinheim, Germany.

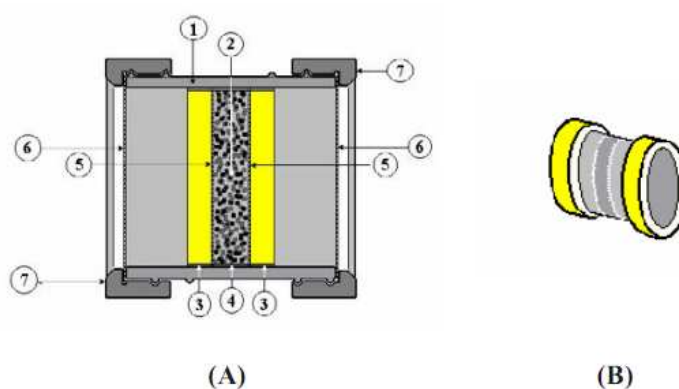
solvated sample on a matrix. The sample is heated to produce the gaseous solution and then it is injected onto the column. Adsorptive sampling involves injection of a solvated sample of air from an adsorptive medium. This means that the medium used to absorb the sample is soaked in solution to remove the sample. The liquid sample is volatilized to a gas at the injection port of the column in this instance. The gas from either sampling method is injected onto a stationary phase column with an inert carrier gas.⁹ As the sample flows through the capillary column, it is heated. Molecules with a high affinity for the stationary phase (based on polarity) will proceed through the column more slowly than those with a lower affinity for it. This separates the mixture into individual components which elute from the column at different times which are relative to their adherence to the stationary phase. Since the inherent properties of the matter are what produces the retention time of the components, the result is a reproducible plot of quantifiable partitions of a complex mixture.

Instrumentation for gas chromatography requires a unique balance of several components to produce peaks which adequately represent the components of a mixture. The process has three steps: injection, separation, and detection. Acquisition of the sample can occur in several ways. A cigarette smoking machine can be used to artificially mimic the mechanism of a person smoking a cigarette. A glass fiber cigarette filter which was attached to the smoking machine can then be submerged in a suitable solvent such as diisopropyl ether or methyl tert-butyl ether.⁷ This solution can then be subjected to either direct injection, which is unadvisable, or the solution can be subjected to headspace sampling. Direct injection as opposed to split sampling is not best in this instance. The high load of non-evaporating tar based products in the cigarette smoke would contaminate the inlet of the gas chromatograph.⁷

⁸ Tang, H., G. Richards, et al. (1988). "Determination of gas phase nicotine and 3-ethenylpyridine, and particulate phase nicotine in environmental tobacco smoke with a collection bed – capillary gas chromatography system." Journal of High Resolution Chromatography (now called Journal of Separation Science) **11**(11): 775.

⁹ Skoog, D. A., F. J. Holler, et al. (2007). Instrumental Analysis. India ed. Brooks/Cole. New Delhi.

This would lead to inaccuracies in runs that occur after the first trial which caused the contamination. A highly concentrated sample, would also lead to disfigurement of the peaks into a “chair” conformation, which hinders the reproducibility and the quantifiability of the results. Another method for sample procurement is the use of a semi-volatile organics collector (SVOC) which acts as an absorbing medium for the particulate and semi-particulate matter (Fig. 4).⁵ This device uses one of several adsorbing media. Success has been made using XAD-4 absorbent resin which makes use of a high surface area and micropores to trap nicotine most efficiently.^{10, 11}



(A) Scheme of the Analyst 2 sampler: 1: glass cylinder (i.d. = 20 mm, double diffusive path length = 10 mm); 2: adsorbent bed; 3: retaining S.S. rings; 4: viewing S.S. ring; 5 and 6: S.S. nets; 7: aluminium screwed rings, retaining the air barriers (consisting of (6) nets);
 (B) General view of Analyst 2 device.

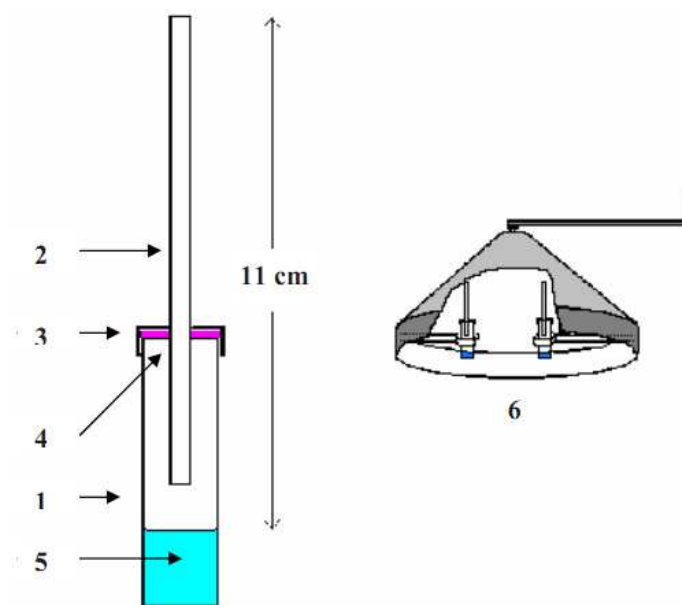
Figure 4: Resin coated adsorbent device (Bertoni et al)

This resin is manufactured by Sigma-Aldrich under the Amberlite brand, and it is a non-polar absorber of hydrophobic molecules--even for molecules which are sparingly soluble in organic

¹⁰ Ogden, M. W., L. W. Eudy, et al. (1989). "Improved gas chromatographic determination of nicotine in environmental tobacco smoke." *The Analyst* **114**(9): 1005-1008.

¹¹ Hengel, M. J., B. K. Hung, et al. (2005). "Analysis of Nicotine in California Air Samples from XAD-4 Resin." *Bulletin of Environmental Contamination & Toxicology* **74**(3): 445-455.

solvents. The pore size is related to the number following the XAD label, and the pore rating of 4 has been determined to provide the best absorbance and desorbance for the analysis of nicotine and 3EP. It corresponds to an average pore diameter of 640 microns. The use of this adsorption technique differs from the glass filter, because it is selective for aromatics, and can be used to collect air samples which did not necessarily come directly from the burning tobacco. This makes it especially useful for detecting 3EP, which may not appear in the glass pack filter of a cigarette smoking machine since it is not produced as much during inhalation. A third type of collection method was created by Bertoni et al to take samples from homes and businesses of the carbon dioxide content in locations with different smoking levels (Fig. 5).⁵ This allows for quantization of the effects that smoking has on the atmospheric carbon dioxide levels. A glass rod inserted in a septum allows for gas to diffuse into the chamber, there a solution of barium hydroxide absorbs the carbon dioxide and can be analyzed by inductively coupled plasma with atomic adsorption spectrometry (ICP-AES) for concentration of barium carbonate.



Structure of the diffusive devices: 1.glass vials (20 mm I.D.x 50 mm height); 2.diffusive path length determining glass tubes (4 mm I.D.); 3.plastic screwed caps; 4.rubber-teflon septum; 5.adsorbing solution; 6.exposure shelter.

Figure 5: Carbon dioxide collection apparatus (Bertoni et al)

Another option for creating a headspace analysis is the use of thermal desorption.^{12, 13} This method uses Tenax or Carboxen C as the sorbent bed which collects the material.^{1, 3, 6} These two absorbing media are comparable to the XAD-4 in terms of hydrophobic interactions and pore diameter. Tenax is company that makes filters of a certain octagonal shaped formation. Carboxen C is an absorbing material usually used in columns designed for liquid chromatography. With the option of headspace analysis, the solid matrix of the adsorption column is heated to volatilize the organics contained within. The now gaseous, desorbed

¹² Baltussen, E., A. Boer, et al. (1999). "Monitoring of nicotine in air using sorptive enrichment on polydimethylsiloxane and TD-CGC-NPD." *Chromatographia* **49**(9/10): 520.

¹³ Ochiai, N., T. Ieda, et al. (2007). "Comprehensive two-dimensional gas chromatography coupled to high-resolution time-of-flight mass spectrometry and simultaneous nitrogen phosphorous and mass spectrometric detection for characterization of nanoparticles in roadside atmosphere." *Journal of Chromatography A* **1150**(1-2): 13-20.

constituents are then injected directly into the gas chromatograph for analysis. This will eliminate the need for a solvent, and possibly eliminate solvent effects, such as “chair” conformations, caused by cooling of the column.

Once the sample is injected, it is subjected to a temperature ramp as it is pushed by the carrier gas (usually helium) through the capillary column. For this type of experiment, a non-polar stationary phase bonded to the capillary column such as dimethylsiloxane is used. With solvent extraction, sometimes a distorted peak occurs which does not conform to a Gaussian distribution, causing problems with quantifiability.⁷ This can be corrected when dissolved with a co-solvent with high molecular weight such as dichloromethane, so solvent trapping occurs, and the problem is lessened.

Solvent trapping works by re-dissolving any straggling molecules and encouraging them to group together with similar molecules. This encouragement comes from the hydrophobic interactions of the sample partition and the stationary phase of the bonded silica column. As the carrier gas pushes the mixture through the column, the molecules are constantly rearranging to the most thermodynamically favorable positioning by sticking to the column with the hydrophobic interactions. When a small solvent with a low boiling point is used, such as the commonly used diethyl ether, the solvent wants to elute from the column so fast that there is not enough time for the rearrangement of the sample material to occur, so the peak stretches out in terms of time. This is the so-called “chair” type peak. With the addition of a bulky co-solvent, the early elution of diethyl ether will still occur, but the sample material can still be dissolved in the relatively ‘slower’ bulky solvent. The bulkier co-solvent cannot be used by itself because it may inadequately dissolve the sample portions to be analyzed. If a small solvent with slightly higher polarity, such as methanol, is used band broadening in space may occur. Spatial band broadening is usually seen with improper injections so the length of the column is filled with solute. This occurs with the polar solvents in non-polar columns because the solvent will ‘wet’

the interior of the column and diminish the number of sites available for the non-polar molecules to bond. This will not allow for the proper rearrangement of the injected sample and produce a wider peak in time. The use of an improper column with this technique can also cause band broadening in space, which, in this case, is the distortion of the peak shape due to solvent interactions with the solute. This can be overcome by using a differently coated precolumn or cooling part of the column below ambient temperature, which sharpens the peaks considerably. By using a column with a more polar coating (less phenyl sites in the siloxane chain) the wetting of the column can be minimized since this precolumn focuses the polar solvent before it can spread out spatially.

To determine what actually is being eluted from the column, a detector is attached at the exit end to produce a numerical representation of the determined change in the analyzed property of the exit gas, such as conductance across the diameter of the exit port. There are three different types of detectors that have been used for nicotine and 3EP analysis, the flame ionization detector (FID), nitrogen-phosphorous detector (NPD), and mass spectrometer (MS). While FID and NPD compare the conductance of the material eluting from the column to the carrier gas baseline, MS actually fragments the molecules and can provide a quick determination of the mass properties of the compound. All of these methods destroy the molecules which come off of the column, preventing further tests on the separated portions. FID is often used for organic analysis, as it provides low detection limits for carbon containing compounds, for which it is selective. Detection limits for nicotine and 3EP are much lower than those detected when using MS.^{6, 14} It works by pyrolyzing an elutant in a hydrogen-oxygen flame and electrically determining the quantity of ions in the resulting flame (Fig. 6).

¹⁴ Lu, X., M. Zhao, et al. (2004). "Characterization of cigarette smoke condensates by comprehensive two-dimensional gas chromatography/time-of-flight mass spectrometry (GC x GC/TOFMS). Part 2: basic fraction." Journal of Separation Science **27**(1-2): 101-109.

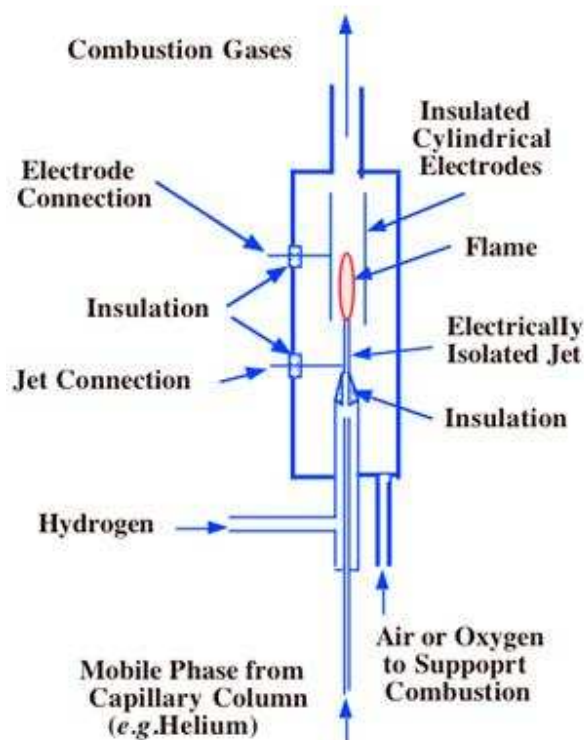


Figure 6: FID diagram. (<http://www.chromatography-online.org/Chrial-GC/images/image135.jpg>)

A detector which is selective for nitrogen and phosphorous ions, the NPD, is useful in this circumstance, since both nicotine and 3EP are both nitrogenous compounds. NPD works similarly to the FID, but it uses an alkali bead to collect the selected ions (Fig. 7). Since NPD ignores aromatic compounds that may obscure peaks detected FID in the gas chromatograph, it is the most common ionic detector used for tobacco analysis.

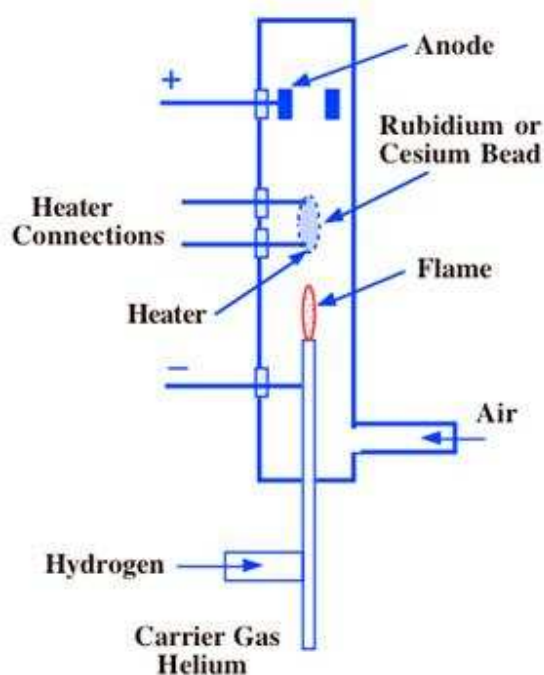


Figure 7: NPD diagram (<http://www.chromatography-online.org/Chrial-GC/images/image136.jpg>)

In contrast to, and occasionally in conjunction with, the ionic conductance detectors, mass spectrometry is a valid choice for detection of the separated gas. While MS gives worse detection limits than the FID or NPD, it has the distinct advantage of partition identification when used in conjunction with GC. This is useful for verification that the portion being analyzed is actually the marker in question. For tobacco based gas chromatography experiments, the most common form of MS used is electron ionization (EI). This mechanism blasts outlet stream with electrons, creating radical and cation pairs from each shattered bond (Fig. 8). The cations can then be sorted by mass to charge ratio by magnetic detectors and time of flight detectors.

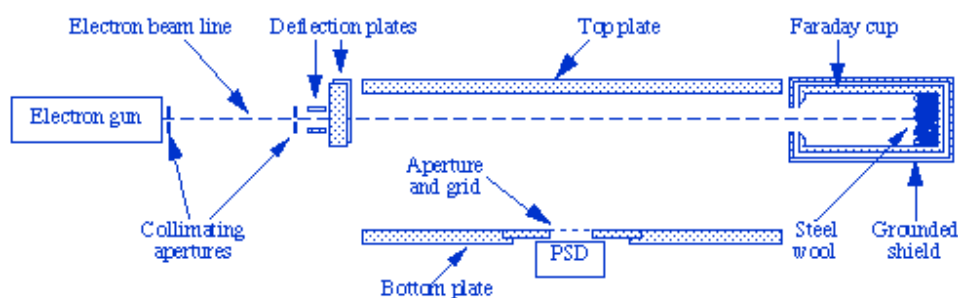


Figure 8: EI-MS diagram (<http://www.ruf.rice.edu/~atmol/images/Mach3.gif>)

The best substitute indicator of nicotine was proven to be 3EP, which produced a high correlation factor.¹⁵ In all of the comparable methods used, the concentration of nicotine detected in the system was higher than the concentration of 3EP, but nicotine samples had higher relative standard deviation in some cases.³ This indicates that the rapid degradation of the nicotine in the presence of UV radiation, in the case of Kuusimaki et al over a 6 hour period, was significant enough to produce strong variations in the result. With different collection methods, a common theme ran throughout. Nicotine concentrations increased from non-smoking indoor environments, to open outdoor air, to indoor smoking environments.^{1, 5} Nicotine was still present in “smoke-free areas.”^{16, 17} Huali et al showed that their collection method using dimethylsiloxane was independent of sample time after the first hour.¹⁸ This contradicts the findings of Baltussen et al (Fig. 9) which chart the concentrations detected in an indoor environment over the course of a workday.¹² Whether the dependence on the time of day is

¹⁵ Rothberg, M., A. Heloma, et al. (1998). "Measurement and analysis of nicotine and other VOCs in indoor air as an indicator of passive smoking." *The Annals Of Occupational Hygiene* **42**(2): 129-134.

¹⁶ Schenker, M., A. C. Roche, et al. (1987). "Collection and analysis of nicotine as a marker for environmental tobacco smoke." *Atmospheric Environment* (00046981) **21**(2): 457.

¹⁷ Williams, D. C., J. R. Whitaker, et al. (1985). "Measurement of Nicotine in Building Air as an Indicator of Tobacco Smoke Levels." *Environmental Health Perspectives* **60**: 405-410.

¹⁸ Huali, Y., G. Songting, et al. (2002). "Trace Analysis of Nicotine in Indoor Air by a SPME Method." *Bulletin of Environmental Contamination & Toxicology* **68**(4): 485-489.

related to increased smoker traffic in the indoor environment or the effects of UV radiation was not determined or discussed by the author.

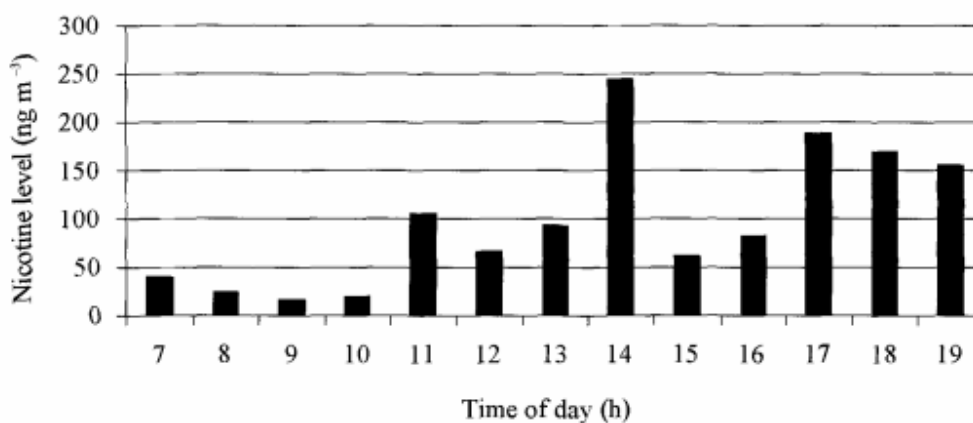


Figure 9: Nicotine concentration is dependent on time of day (Baltussen et al)

Both of these experimenters used similar desorption methodology. The difference may be due to Huali et al using insufficient sampling or sampling during the same part of the day, thus decreasing the value of the results. Carbon dioxide sampling only showed a small increase due to the presence of smokers.¹ Different adsorbants both produce strong quantifiable results, but they are not comparable due to different analytical methods used. NPD and FID both produced stronger results than MS detection techniques, although both produced detectable quantities for all comparable results.

Table 1: Average detection limits (Data sources 1-3, 6, 15)

Comparator of Detection Limits				
	Nicotine		3-Ethenylpyridine	
Desorption Method	Solvent ($\mu\text{g}/\text{m}^3$)	Thermal ($\mu\text{g}/\text{m}^3$)	Solvent ($\mu\text{g}/\text{m}^3$)	Thermal ($\mu\text{g}/\text{m}^3$)
	0.1155 ± 0.1	0.1534 ± 0.3	0.1 ± 0.1	Insufficient Data
Detection Method	Ionizing ($\mu\text{g}/\text{m}^3$)	Mass Spec. ($\mu\text{g}/\text{m}^3$)	Ionizing ($\mu\text{g}/\text{m}^3$)	Mass Spec. ($\mu\text{g}/\text{m}^3$)
	0.0908 ± 0.1	0.1544 ± 0.3	0.0305 ± 0.04	0.108 ± 0.1

By compiling results from papers with similar methods, a list of average detection limits can be made (Table 1). This table shows that, for the data sources used, a number of conclusions can be made. Although there was little work which was of a comparable nature to the others made for 3EP thermal desorption, each of the detection limits for 3EP is lower than those for the nicotine counterparts. In some cases, especially in the case of the ionizing detection method, the standard deviation of the data was significantly lower for 3EP compared to nicotine. This indicates that the use of 3EP as a marker for tobacco smoke will produce more precise results. As expected, the ionizing detection methods produced lower detection limits than the mass spectrometry related detection methods. This exemplifies the trade-off between strong detection limits from a conductance type detector and the accuracy boost from a mass analyzing detector. Although solvent desorption from the solid media produces better results in terms of raw detection limit and precision of the reading, no comparison can be made for 3EP since there was insufficient data for thermal desorption methods.

Although smokeless environments contained about ten times smaller concentrations of nicotine and 3EP, the presence of nicotine in the atmosphere is unavoidable. Since all of the experiments occurred in nations which have restricted the use of tobacco products, little can be concluded about the effects experienced in nations with less restrictive anti-smoking legislation. Adsorption-desorption techniques were shown to produce higher total yields of nicotine

compared to headspace analysis techniques, so it can be concluded that this methodology is a better option for quantification of nicotine levels. Since the two classes of detectors have different pros and cons, neither is necessarily better than the other. The choice between these two detectors is situational.

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