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Development and Initial Application of Low-Molecular Weight Organic Acids and Inorganic Ionic Species in Aerosol Particulate Matter via Ion Chromatography

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Development and Initial Application of Low-Molecular Weight Organic Acids and
Inorganic Ionic Species in Aerosol Particulate Matter via Ion Chromatography

by

Clarissa D. Karpinski

An undergraduate honors thesis submitted in partial fulfillment of the
requirements for the degree of
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in
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Thesis Adviser

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Abstract

Air pollution, especially particulate matter, is a widespread environmental and public health risk. In this work, a method has been developed to separate, resolve, and quantitate monovalent anionic and cationic organic acids in aerosol particulate matter through ion chromatography (IC). The standard samples were analyzed on a Dionex ICS-5000 Ion Chromatography System with suppressed conductivity detection, and calibration curves for all analytes were created. A preliminary tobacco smoke sample was also analyzed. This method may be applied to the analysis of atmospheric particulate matter, as well as tobacco smoke particulate matter, in order to determine and quantitate primary anions and cations.

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Introduction

1.1 Research Motivation

1.1.1 Health Effects of Particulate Matter

Air quality is directly related to the condition of the general public health. Polluted air may be caused by natural sources, such as volcanic eruptions or smoke from forest fires, or by human sources. While there are many pollutants created by human activity, the primary air pollutants of concern include ozone, sulfur dioxide, nitric oxides, and carbon dioxide.¹ The emissions of sulfur and nitrous oxides, including sulfur dioxide, nitrite and nitrate ions, may react with water in the atmosphere to create acidic compounds and that can be transported or deposited through wet (i.e. rain, snow) or dry (i.e. particles, gases) methods.¹ The United States Environmental Protection Agency (EPA) has named six common air pollutants which may cause damage to the environment and/or to human health. These include the previously mentioned pollutants, as well as particulate matter and lead.² Particulate matter, or PM, are small solid or liquid particles that are suspended in the air and may differ in size. The two sizes of interest are PM_{2.5} and PM₁₀; particles that are 2.5 micrometers or less in diameter are classified as “fine” and those that are between 2.5 and 10 microns in diameter are “coarse” particles. When fine particles are breathed in, their small size allows them to travel through the upper respiratory tract where they can be deposited deep into the lung tissue and accumulate. This deposition is a great cause for concern, as scientific studies have shown that air pollution, especially PM_{2.5}, can create significant health problems, such as chronic respiratory issues, irregular heartbeat, and decreased lung function.³

An abundant of fine particulate matter is also created through the combustion of tobacco and cigarette products. The health effects of environmental tobacco smoke, or ETS, and air pollution mirror each other in terms of diseases related to cardiovascular and respiratory

functions.⁴ Smoking is the primary cause of preventable death, yet with over one billion smokers worldwide, up to half of the current users will ultimately die from tobacco-related causes.⁵ There are nearly six million deaths per year caused by smoking; over five million fatalities were directly caused by tobacco use, and the remaining deaths are the consequence of non-tobacco users being exposed to secondhand smoke.⁵ According to the World Health Organization, an expected one billion deaths will occur in the 21st century if the smoking epidemic continues as it has been. It is widely known that smoking cigarettes for many years typically results in lung cancer. Smoking causes damage to nearly every organ in the body and may also cause cancers of the blood, bladder, pancreas, liver, kidney, and more.⁶ Prolonged tobacco use is also the source of many chronic diseases such as coronary heart disease, asthma, chronic obstructive pulmonary disease, and can also compromise the immune system and respiratory function.

There are numerous origins of particulate matter in the atmosphere including natural causes, and human sources such as environmental tobacco smoke. A brief report found that cigarette smoke caused ten times more particulate matter concentrations in an indoor environment than an idling eco-diesel truck engine.⁷ It is evident that smoking and tobacco use are not only a great threat to general public health, but to the health of the environment as well. Clearly, there is a need to investigate the constituents of particulate matter, in the atmosphere and in tobacco smoke, in order to combat the number of associated environmental and public health issues.

1.1.2 Nicotine and Tobacco Chemistry

A complex mixture of chemicals is created during the combustion process of tobacco. Cigarettes, in general, are composed of the tobacco, a filter, and cigarette paper. The grade of tobacco used can vary the levels of nicotine, other chemical additives, and pH values depending

on how the tobacco was harvested and cured.⁸ When a cigarette is smoked, a sequence of chemical reaction processes takes place and three types of smoke are created through the puffing and smoldering of a cigarette: mainstream smoke, sidestream smoke, and environmental tobacco smoke. When a user puffs a cigarette, the smoke that is inhaled is called mainstream smoke. In between puffs, when the cigarette is smoldering, sidestream smoke is created. Environmental tobacco smoke (ETS), or secondhand smoke, is formed when the user exhales a fraction of mainstream smoke, which combines with sidestream smoke.⁸ In whole mainstream smoke, there are millions of small liquid droplets suspended in a gaseous system; the liquid droplets of the smoke are defined as the particulate phase and the remaining components are the vapor phase of the smoke aerosol.⁹

Many factors influence the relative chemical composition levels in mainstream smoke, including the manner in which the cigarette is puffed, tobacco blend and/or type, and tobacco preparation. Nicotine, the addictive compound in tobacco, is primarily contained

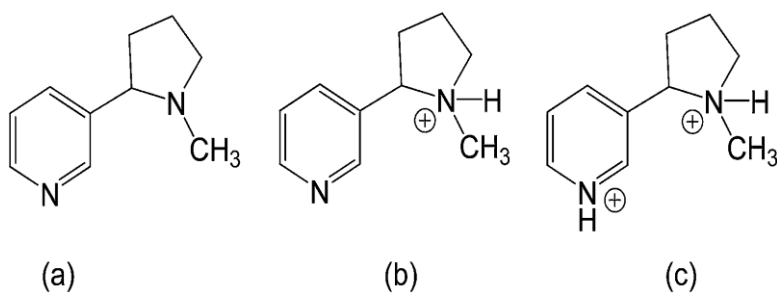


Figure 1. Free base (a), monoprotonated (b), and diprotonated (c) nicotine¹⁰

in the particulate phase of the emissions, and can be found in three forms (Figure 1): unprotonated (free base), monoprotonated, and diprotonated.¹¹ The amount of nicotine, which is itself a base, in each of the three forms heavily depends on the pH of the particulate phase solution. The more acidic the solution is, the greater the fraction of protonated nicotine molecules. Equally, as the solution increases its basicity and pH level, the fraction of unprotonated nicotine increases. Although all forms of nicotine are able to dissolve into the

blood and lung tissue, unprotonated nicotine is volatile and deposits into the respiratory tract at a higher percentage than the two protonated forms.¹² Greater rates of nicotine deposition increase the addictive properties of the compound by supplying the brain with nicotine at a faster rate. It is important to determine the pH level of the particulate phase in order to define the fraction of unprotonated versus protonated nicotine. However, due to the chemical properties of tobacco smoke particulate phase, unconventional methods are required to test the pH of the solution to obtain the fraction of unprotonated nicotine.^{12, 13} These methods are complex and are beyond the scope of this project.

The speed at which inhaled nicotine from the particulate phase of tobacco smoke evaporates and deposits in the respiratory tract is directly proportional to the fraction of unprotonated nicotine in the smoke.¹⁴ The value of this fraction in tobacco smoke is dependent on the total ratio of acids to bases. There are naturally occurring acids in tobacco, such as acetic, formic, and propionic acid, which allow nicotine to be in its protonated and non-volatile form. Of the fraction of chemicals that are in the particulate phase of tobacco smoke, 0.6% of organic acids and 0.9% of other inorganic compounds are present.⁸ There is little modern research on the components and their concentrations in cigarette smoke particulate matter, especially regarding organic acids and additional compounds, such as small inorganic ions. Analysis of the particulate matter, whether in tobacco smoke or in the atmosphere, requires chromatography, which is the general term used to describe a wide range of chemical separation techniques.

1.2 Analytical Review and Relevant Chemistry

1.2.1 Chromatography Mechanisms

The basic principle of chromatography includes the distribution and separation of components in a mixture between a mobile and a stationary phase. This distribution allows one

to analyze the individual constituents that make up the complex mixture. A sample of substance to be separated is dissolved in the mobile phase, which is sent through another material called the stationary phase. Based on the size of the molecules and the partition coefficient between the two phases, the various components of the mixture, called the analytes, are separated by the speed at which they travel through the stationary phase. The partition coefficient describes the distribution of the analyte between the mobile and stationary phases, and is defined as the ratio of the concentrations of the analyte in both phases at equilibrium. There are several classes of chromatography, such as liquid, gas, and paper chromatography, which are separated based on the physical state of the two phases.¹⁵ Ion chromatography, a type of liquid chromatography, is used to separate ionic, or charged, compounds in a mixture. In this case, the mobile phase is a buffered aqueous solution called the eluent that carries the sample through a charged stationary phase, which is a column containing a polymer resin. Once the sample mixture is separated, the individual analytes are sent to a detector for further analysis.

1.2.2 Ion Chromatography Background

Ion chromatography is an especially useful tool in the examination of the ions present in atmospheric and tobacco smoke particulate matter. A Dionex-5000 Ion Chromatography System (ICS) was utilized in this work. There are four main parts to the ion chromatographic system: the pump, the eluent generator (EG), the detector/chromatography (DC) compartment, and an autosampler (AS). The pump delivers the eluent through the chromatographic system, which may be done in an isocratic or gradient flow method. Isocratic ensures that the concentration of the mobile phase is constant throughout the analysis, and gradient flow allows a varying concentration to be distributed. The eluent generator produces highly pure acidic or basic component to be used as the mobile phase from a disposable cartridge, and uses a reservoir of

deionized water to appropriately dilute the mobile phase. A continuously regenerating trap column (CR-TC) within the EG compartment is responsible for removing superfluous compounds from the deionized water source. The detector/chromatography module is composed of conductivity detectors (CD), injection valves, columns, and suppressors, and provides a temperature-controlled atmosphere for its constituents. The suppressor decreases the amount of background noise recorded and the CD component detects the electrical signal acquired from the sample. The autosampler allows for multiple samples to be analyzed sequentially.

Experimental Methods

2.1 Materials and Instrumentation

2.1.1 Materials

Deionized water, obtained from a Millipore Milli-Q water purification system with a specific resistance near 18 M Ω , was used to dilute the eluent. Eluent generator cartridges were provided by Dionex; potassium hydroxide (KOH) and methanesulfonic acid (MSA) were used to analyze anions and cations, respectively. Potassium chloride, ACS reagent (KCl), sodium chloride 99.0+%, ACS reagent (NaCl), sodium sulfate, 99.0+%, ACS reagent (Na₂SO₄), ammonium formate, 97% (NH₄CHOO), and isopropyl alcohol, 99.9% (IPA), were supplied from Sigma-Aldrich. Ammonium chloride, 99.70% (NH₄Cl), and potassium nitrite, assay (KNO₂) were supplied through JT Baker, Incorporated. Potassium nitrate, 99.99% (KNO₃), was supplied through Aldrich Chemical Company. Enzyme grade potassium acetate, 99% assay (KOAc), was supplied through Fischer Scientific. All reagents and solvents were used as received from their respective suppliers and stored as per the manufacturer recommendation.

2.1.2 Instrumentation

All ionic standard samples and smoke samples were analyzed with a Dionex-5000 Ion Chromatography System with suppressed conductivity detector. A continuously regenerating trap column was utilized for the analysis of anions only. The data obtained was examined with the associated software program, the Dionex Chromeleon Chromatography Data System.

2.2 Methods

2.2.1 Method Development

Several cationic organic acids and anionic inorganic species were analyzed as calibration standards. The species were chosen by studying pertinent literature on the commonly found cations and anions in environmental particulate matter, as well as in tobacco smoke. Acetic and formic acids were commonly reported in cigarette smoke samples^{16, 17, 18, 19}; chloride, nitrite, and nitrate ions have been reported in trace amounts.¹⁶ Anions including sodium, potassium, and ammonium were also reported in literature.¹⁶ The emissions of sulfur and nitrous oxides, including sulfur dioxide, nitrite and nitrate ions, affect environmental and human health. These standards solutions were diluted to various concentrations, ranging from 0.5 ppm to 50 ppm, and mixed with isopropyl alcohol (IPA) to obtain a solution that was 95% IPA. These standard stock solutions were analyzed, individually and in a cationic or anionic mixture, via ion chromatography in order to create a personal library of ionic compounds to use as a reference in the future analysis of environmental or tobacco smoke particulate matter samples.

This method was developed to discover what specific parameters allow for the optimal separation and resolution of the species in question. These parameters consist of the eluent concentration and gradient profile, temperature, column flow rate, and overall sample run time. References to similar journal articles gave a starting point in regards to establishing the various

parameters. Testing of these parameters was completed by analyzing standard sample solutions of the target organic acids and inorganic ionic species several times, at many different values of the concentration gradient of the eluent, rate of the column flow, sample run time, temperature, etc.

For the anionic standards, the optimal parameters were found by using a concentration gradient profile for the eluent (Table 1), a cell and column temperature of 45°C, a compartment

Table 1. Eluent concentration gradient

Time (min.)	Concentration (mM)
0.0	1.0
5.0	5.0
10.0	10.0
15.0	15.0
20.0	32.0

For anions only

temperature of 35°C, an injection volume of 25 µL, with a total run time of 30 minutes. The current was set at 80 mA, and the flow rate was set to 1.0 mL/min. The ideal parameters for the cationic standards involved an isocratic concentration for the eluent, MSA, at 20 mM.

An injection volume of 25 µL was used with a run time of 10 minutes. The flow rate was set to 1.0 mL/min with a current of 59 mA. The temperature was not controlled.

2.2.2 Cigarette Sampling

The cigarette samples were first manually smoked into a 1 liter capacity Tedlar PLV Gas Sampling Bag in a 4 liter capacity chamber. For each smoking event, two cigarettes were simultaneously smoked for 75 mL, with 2 second puffs (35 mL per cigarette) at puff intervals of 1 minute. Approximately nine puffs were taken from each cigarette. Cigarettes were conditioned to 24°C +/- 1°C and 64% +/- 2% room humidity (RH). Similar methods are described elsewhere.⁷ These smoke samples were subsequently titrated with a strong acid or strong base. The purpose of the titration is to determine the relative concentrations of nicotine to organic acids in tobacco smoke. The titrated solutions were diluted to a certain degree and dissolved in 95% isopropyl alcohol (IPA), as the standards, to reduce matrix effects. A small aliquot of the

samples were analyzed several times to ensure their reproducibility and quality. The spectra were then analyzed via the Dionex Chromeleon software program. Quality assurance and quality control (QA/QC) methods were employed for the purpose of confirming the data collected is true and accurate. Blank samples of deionized water and 95% IPA were ran to ensure extraneous compounds were off the column, internal standards were used to gauge and correct instrument efficiency, and multiple samples were also ran to confirm reproducibility. Instrument calibration was performed by using reference standards to increase the precision and accuracy of the ion chromatography system.

Results and Discussion

3.1 Anions

A calibration curve for an anionic mixture (Figure 2), including nitrite, nitrate, sulfate, chloride, acetate, and formate ions, was created using concentration values of 0.5, 1.0, 5.0, 20.0, and 50.0 mg/L. The calibration results for each analyte returned R^2 values ranging from 0.9985 to 1.000. The limits of detection (LOD)

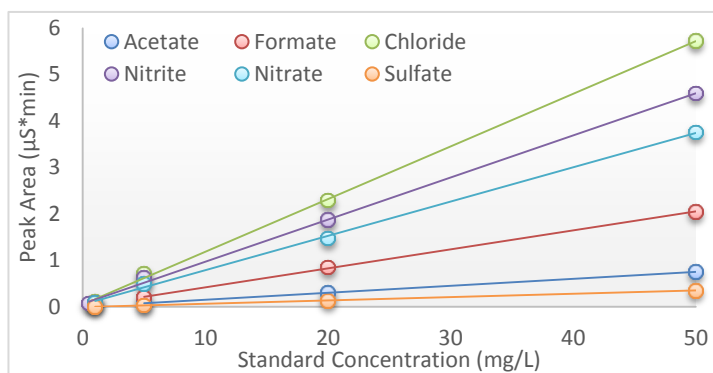


Figure 2. Anion calibration curve

Table 2. Anion calibration results

Ion	RT (min)	%RSD	LOD (mg/L)
AcO ⁻	8.19	0.356%	1.09
CHOO ⁻	9.05	0.332%	2.26
Cl ⁻	12.10	0.049%	2.16
NO ₂ ⁻	14.17	0.137%	2.54
NO ₃ ⁻	19.46	0.320%	3.20
SO ₄ ⁻²	23.22	0.045%	0.18

for the anionic standards ranged from 0.18 mg/L to 3.20 mg/L, as shown in Table 2. There is a clear correlation between the R^2 value and the limit of detection; a lower LOD typically indicates an increased R^2 value. Figure 3 depicts the overlaid

chromatograms for all anion concentration values, from 0.5 mg/L to 50 mg/L. The peaks shift slightly to the right with increasing concentration; however, the relative area and peak height is linearly increasing as well. With clear and well-separated peaks, these results confirm the quality of the instrument method created.

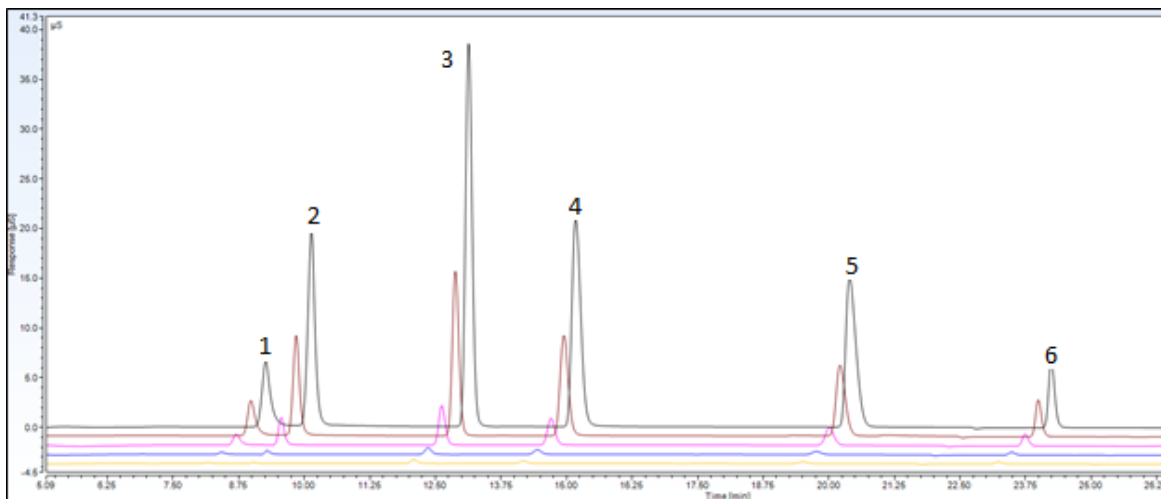


Figure 3. Anion calibration chromatogram, overlaid. The anions were acetate (1), formate (2), chloride (3), nitrite (4), nitrate (5), and sulfate (6).

3.2 Cations

A calibration curve containing a mixture of sodium, potassium, and ammonium ions was created using concentration values of 0.5, 1.0, 5.0, 20.0, and 50.0 mg/L (Figure 4). The R^2 values

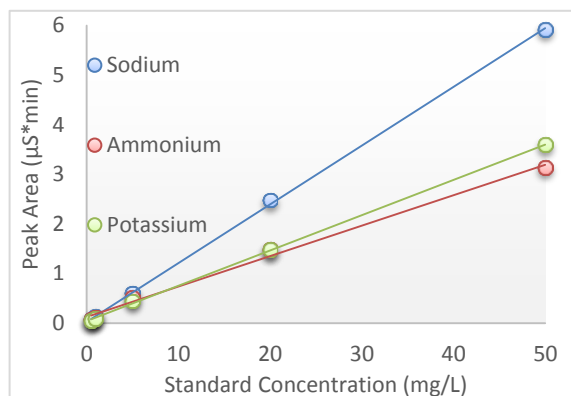


Figure 4. Cation calibration curve

returned ranged from 0.9945 to 0.9997. As with the anions, a lower R^2 indicated a higher limit of detection. For example, ammonium returned the highest LOD value of 5.377 mg/L, and also procured the smallest R^2 value (0.9945). These detection limits, as well as the per cent RSD value, are found in Table 3. The detection limits for the

other two cations, sodium and potassium, yielded values near 1.3 mg/L.

Although sodium and potassium had lower limits of detection, they also had an increased per cent RSD value, which indicates a slightly higher variability in the data. Figure 4 depicts the overlaid chromatogram for the three cation analytes, with concentration values ranging from 0.5 mg/L to 50 mg/L.

Table 3. Cation calibration results

Ion	RT (min)	%RSD	LOD (mg/L)
Na ⁺	4.503	0.169%	1.270
NH ₄ ⁺	5.123	0.087%	5.377
K ⁺	6.543	0.264%	1.407

With increasing concentration, each analyte peak increases in height and area, and also becomes better defined.

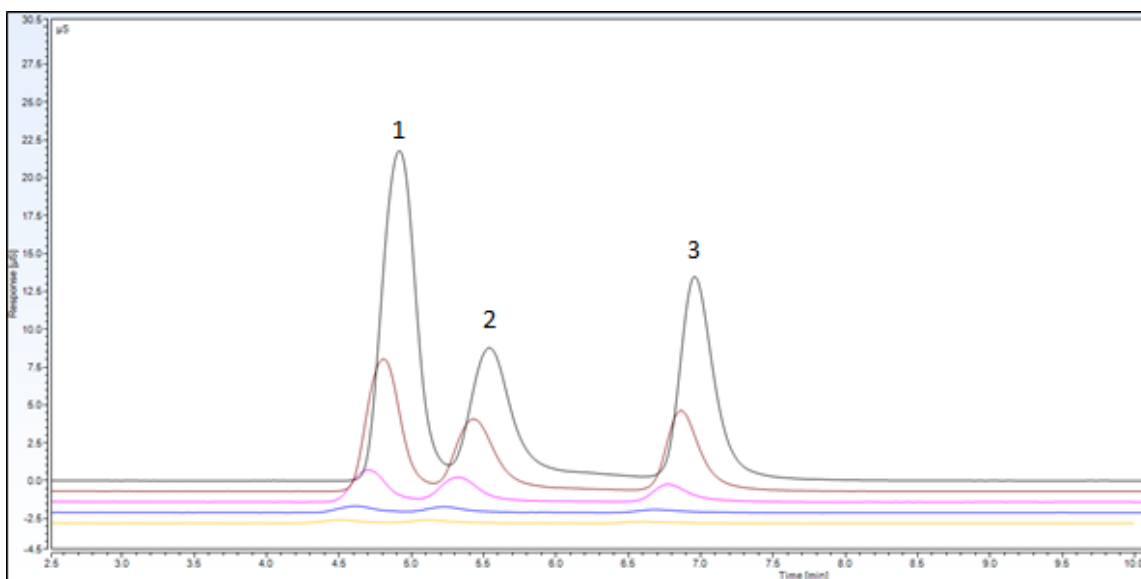


Figure 3. Cation calibration chromatogram, overlaid. The cations were sodium (1), ammonium (2), and potassium (3).

3.2 Preliminary Tobacco Smoke Analysis

A tobacco smoke sample was qualitatively analyzed for its constituents. As shown in Figure 6, several monovalent ionic species were found. These include acetate, formate, chloride, nitrite, and sulfate. Peak (5) was listed as either nitrite or sulfite, as that particular peak was unable to be positively determined.

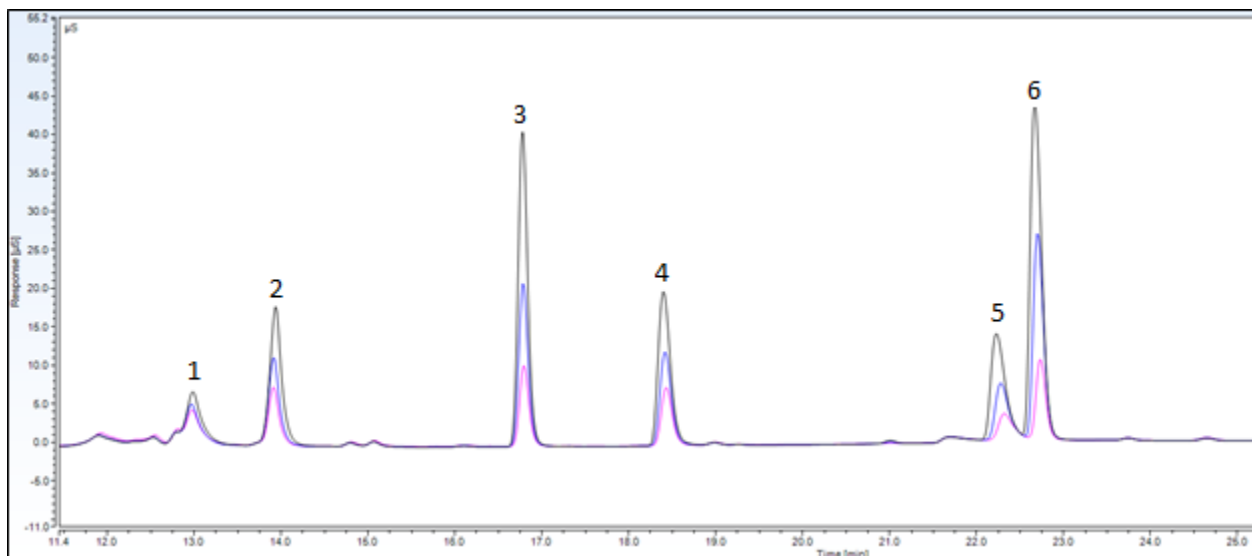


Figure 6. Preliminary tobacco smoke sample chromatogram, overlaid to show standard additions. The analytes found were acetate (1), formate (2), chloride (3), nitrite (4), nitrate/sulfite (5), and sulfate (6).

While the quantity of these ionic species was not determined, this preliminary sample confirms the specific anions in tobacco smoke, which may serve as a stepping stone into further analysis and quantitation.

Conclusions

A simple method has been developed for the determination and quantitation of monovalent low-molecular weight organic acids and inorganic ionic species in aerosol particulate matter through ion chromatography with suppressed conductivity detection. This method has been developed for six anions, Cl^- , AcO^- , CHOO^- , NO_2^- , NO_3^- , and SO_4^{-2} , as well as three cations, Na^+ , K^+ , and NH_4^+ . The study of particulate matter in the atmosphere, caused by increasing air pollution and mainstream tobacco smoke, is of great importance to combat the detrimental environmental and human health effects it produces.

Future Work

The method developed in this work may be applied to the analysis and quantitation of mainstream cigarette smoke by ion chromatography for relevant organic acid ions and other inorganic ionic species. Determination of these concentrations will allow for further research of the pH level of the particulate phase in tobacco smoke, with the intent to describe the fraction of unprotonated and protonated nicotine in tobacco smoke.

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Appendix

Table 4. Salts used as standard analytes

Compound	CASRN	Structure
Sodium Chloride	7647-14-5	$\text{Na}^{\oplus} \text{Cl}^{\ominus}$
Potassium Chloride	7447-40-7	$\text{K}^{\oplus} \text{Cl}^{\ominus}$
Ammonium Chloride	12125-02-9	$\text{NH}_4^{\oplus} \text{Cl}^{\ominus}$
Ammonium Formate	540-69-2	$\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^- \text{NH}_4^+$
Potassium Acetate	127-08-2	$\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^- \text{K}^+$
Potassium Nitrite	7758-09-0	$\text{K}^+ \text{O}=\text{N}-\text{O}$
Potassium Nitrate	7757-79-1	$-\text{O}-\overset{\text{O}}{\parallel}{\text{N}}^+-\text{O}^- \text{K}^+$
Sodium Sulfate	7757-82-6	$\text{Na}^+ \text{O}^- \text{Na}^+ \text{O}=\text{S}(\text{O})_2 \text{O}^-$

CASRN = *The Chemical Abstract Services Registry Number*