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A LOOK AT CONTEMPORARY ION CHROMATOGRAPHY

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SUMMARY

The principles and historical development of ion-exchange chromatography are discussed briefly. Modern ion chromatography includes ion-exchange, ion-pair, ion-exclusion and the chromatography of ion–organic complexes. Each is explained briefly. The major detection systems for ion chromatography are outlined: conductivity (suppressed and non-suppressed), direct and indirect spectrophotometry, spectrophotometry with a post-column reactor, electrochemical, and differential refractometry. The question of isocratic *vs.* gradient elution is examined briefly. Recent studies on the selectivity of ion-exchange resins are presented. Several examples are given of recent separation methods from the author's laboratory. These include the separation of weak acids by ion-exclusion chromatography, the use of additional ion-exchange columns to enhance the detection of carbonic acid by conductivity, and the determination of metal cations by complexation and subsequent chromatographic separation.

INTRODUCTION

Ion-exchange chromatography has actually been used for the separation of both inorganic and organic ions for many years. However, the separations often took a long time and required the collection of fractions for subsequent analysis. Automatic spectrophotometric detection of separated metal ions has been used at least since 1971[1,2]. A complete separation of the rare earch metal ions using spectrophotometric detecton after a post-column reaction was achieved in 1974[3] and a much improved separation was published in 1979[4].

In 1975, Small *et al.*[5] invented a novel ion-exchange chromatographic method using a conductivity detector. This method used an ion-exchange "separator" column with second ion-exchange "suppressor" column placed in series to greatly reduce the background conductivity. This paper was an important milestone because for the first time ever it made possible the rapid separation and determination of common anions and the alkali metal and alkaline earth cations.

In 1979 and 1980, Gjerde and co-workers[6–8], devised a chromatographic system for common anions and cations that used a conductivity detector and did not require any suppressor column. This was accomplished by packing the separation column with a resin of lower exchange capacity than had been used previously. This made

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it possible to use a very dilute eluent (typically around $5 \cdot 10^{-4}$ M sodium benzoate or potassium acid phthalate) with a low background conductivity for the separation of anions. A dilute solution of nitric acid or ethylenediammonium nitrate was used to separate metal cations and the *decrease* in conductivity was measured.

The name, "ion chromatography" was initially coined for the original system for ion-exchange chromatography using conductivity detection and a chemical suppressor. However, ion chromatography is now used in a much broader context and refers to any reasonably efficient chromatographic separation of ions using an automatic detector.

SYSTEMS AND DETECTORS FOR ION CHROMATOGRAPHY

Since the "early" work on ion chromatography in the late 1970s, many new detectors have been used and important refinements have been made in the systems using conductivity detectors. For example, highly efficient ion-exchange membranes that are continuously regenerated have replaced the bulky suppressor columns that were first used in suppressed ion chromatography.

Table I summarizes the methods of detection most used in conjunction with ion chromatography on either an anion-exchange or a cation-exchange column. In the direct detection methods a sample ion passing through the detector increases the signal. In indirect methods the detector monitors the concentration of an eluent ion. Since the resin exchanges one ion for another, the eluent ion concentration is reduced when a sample component passes through the detector, thereby reducing the signal.

The conductivity detector, in conjunction with an ion-exchange suppressor or not, continues to be the most widely used detector for ion chromatography. For example, a mixture containing fluoride, chloride, nitrate, hydrogen, phosphate, bromide, nitrate and sulfate, each at low ppm concentration, can easily be resolved in 10 min or less. Samples containing very low concentrations of the alkali metal ions plus ammonium can be separated even more quickly.

Indirect spectrophotometry can be an exceptionally sensitive detection method. For separation of inorganic anions, an eluent such as sodium molybdate or potassium acid phthalate is used and a wavelength is chosen where only the eluent absorbs. With modern detectors a sensitivity setting of 0.001–0.003 a.u.f.s. can be used. Under appropriate conditions, anions such as chloride, nitrite, bromide, nitrate and sulfate can be detected at concentratrions well below 1 ppm each[9].

Detector	*Mode*	*Ions detected*	*Selectivity*
Conductivity	Suppressed	Anions, cations	General
	Non-suppressed, direct of indirect	Anions, cations	General
Spectrophotometric	Direct	Anions, cations	Some selectivity
	Indirect	Anions, cations	General
	Post-column reactor	Mostly cations	General or selective
Refractive index	Indirect	Anions, cations	General
Fluorescence	Indirect	Anions, cations	General
Electrochemical	Direct	Mostly cactions	Selective
Atomic spectroscopy	Direct	Mostly cations	Selective

A post-column reactor, combined with spectrophotometric detection of the reaction product, is capable of great versatility. Metal cations are detected simply by mixing the column effluent with a buffered color-forming reagent and passing through a detector cell. The detection can be general, or it can be selective for certain ions by judicious choice of the reagent and conditions for the post-column reaction.

TYPES OF ION CHROMATOGRAPHY

Perhaps the most obvious way of doing chromatography is to use a high-performance anion- or cation-exchange column. However, it is also possible to use a bonded-phase silica column of the type commonly used in high-performance liquid chromatography (HPLC). By incorporating an organic ion in the eluent of opposite charge to the sample ions, the HPLC column now functions as an effective column for ion chromatography. Although there can be subtle differences in the mechanism, the following names have been used to describe this general type of ion chromatography: ion-interaction chromatography, ion-pair chromatography, dynamic chromatography, and mobile-phase ion chromatography (MPIC).

The ability to use a conventional HPLC column has been cited as an advantage of this latter form of ion chromatography. However, the performance of permanent ion-exchange columns has been increasing dramatically. The quality of separations attainable by the two forms of ion chromatography is comparable.

ISOCRATIC OR GRADIENT ELUTION?

Until recently most ion-chromatography separations have been carried out with a fixed eluent (isocratic elution). Most of the detectors commonly used respond to changes in eluent concentration, making gradient elution very difficult. However, gradient elution has been used very successfully for selective electrochemical detectors[10] and for spectrophotometric detection after a post-column reaction[4]. In these instances, changes in eluent concentration or pH have little or no effect on the detector signal.

Dionex has recently developed membrane suppressor units that can handle a rather larger increase in the concentration of a basic eluent such as sodium hydroxide. Some stunning gradient separations of anions have been obtained[11].

Gradient elution is certainly a nice option to have available; it does tend to maximize the resolving power of ion chromatography. However, gradient separations can take longer if the time required to get ready for the next run is taken into account. It has been said that gradient separations can lead to confusion on quantitation unless suppression is precisely coordinated with changes in eluent[12]. Some recommend gradient elution primarily as a scouting or survey technique for complex samples.

ION EXCHANGE SELECTIVITY

An understanding of the factors that affect the selectivity of ion exchanges for various ions is useful in designing resins that will give better separations. It is also of theoretical interest to know how various parameters affect ion-exchange selectivity.

In this connection, ion chromatography is an excellent way to obtain retention data for different ions. Sevenich and Fritz[13] published extensive data on the relative retention of various cations. Plots of log retention time (or log k') *vs.* log of eluent ion concentration were linear and showed that the average charge of the metal cation taken up by the resin had the theoretical value of +2 or +3.

Some of the factors that affect the selectivity of resins for anions have been studied in the author's laboratory. The incorporation of butyl or hexyl groups instead of the methyl groups generally used in quaternary resins of the type polymer–C_6H_4–$CH_2N^+R_3A^-$ greatly increased the retention of ions like nitrate, iodine and tetrafluoroborate relative to chloride[14,15]. For anion exchangers prepared by coating a polymeric resin with cetylpyridinium chloride, the retention of nitrate was much greater on a polyacrylate resin than on a polystyrene polymer[16].

The effect of "spacer arms" on the selectivity of anion-exchange resins for various anions has been studied[17]. Polystyrene resins were functionalized with carbon chains of varying lenth between the benzene ring and the nitrogen of the quaternary ammonium group. For several anions, the effect of spacer arm length on the retention times was minimal. But, for other ions, a significant change was observed, as shown in Fig. 1.

The effect of the larger alkyl groups on the greater relative retention of poorly hydrated anions such a bromide, iodide and nitrate has been attributed to stronger ion pairing resulting from disruption of the water structure by these anions and by tightening of the water around the ion pair by the larger alkyl group[14,15]. It is also likely that the ion pair consisting of the quaternary ammonium group of the resin and the exchangable anion is in close proximity of the polymeric resin matrix. The

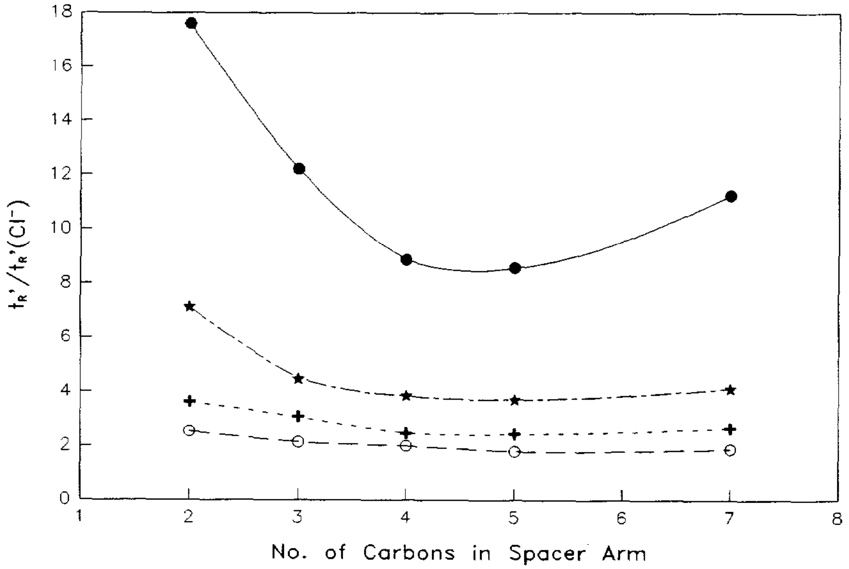

Fig. 1. Effect of spacer arm length on the retention times of anions relative to the retention time of chloride in polystyrene anion-exchange resins. Anions: (○ – – ○) bromide, (+ – – +) nitrate, (★– – –★) chlorate, (●——●) iodide.

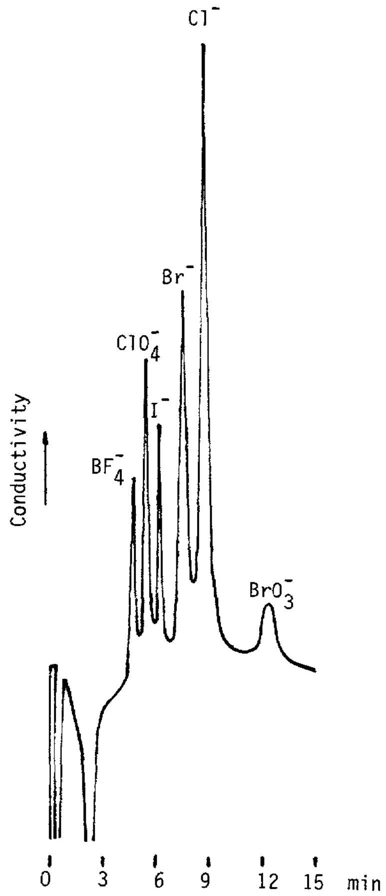

Fig. 2. Separation of anions on a Spherisorb alumina column, 5 cm × 4.6 mm. Conditions: eluent, 0.01 *M* acetate (pH 4.6); flow-rate, 2.0 ml/min; 20 ppm of each anion, conductivity detection.

interaction between the ion pair and the resin matrix will be more favorable as the charge becomes more diffuse and the ion pair becomes more hydrophobic[14,15]. A spacer arm might be expected to reduce this interaction between the ion pair and the resin matrix. This could explain the reduced affinity for ions like iodide by resins with longer spacer arms.

Striking differences in selectivity can sometimes be achieved by using an entirely different type of ion exchanger. At acidic pH values, alumina functions as an anion exchanger. The selectivity of an alumina column for inorganic anions is entirely different than for the quaternary ammonium columns that are generally used. In fact, Schmitt and Pietrzyk[18] showed that the order of elution for halide ions is precisely the opposite on an alumina column as it is on a quaternary ammonium resin column. A separation of several anions on an alumina column is shown in Fig. 2[19].

ION-EXCLUSION CHROMATOGRAPHY

Hydrophilic molecular compounds are often difficult to separate by conventional bonded-phase liquid chromatography. Ion-exclusion chromatography (IEC) provides an attractive way to separate hydrophilic organic compounds and a number o molecular inorganic substances. The separation column is usually a cation-exchange column in the H^+ form, or occasionally an anion-exchange column. The separation excludes ions but allows molecular substances to partition between the mobile phase and stagnant mobile phase inside the ion-exchange resin. In pure IEC the distribution ratios of the sample compounds range from 0 to 1, but there can also be sorption effects.

The eluent in IEC is often water alone. For the separaton of carboxylic acids,

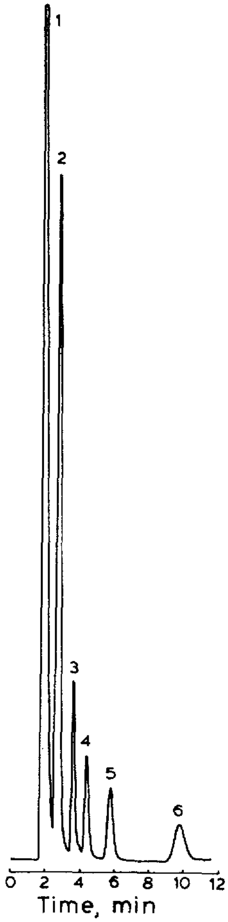

Fig. 3. Ion-exclusion chromatographic separation of carboxylic acids using 0.5 m*M* benzoic acid in water–acetonitrile (95:5) and conductivity detection. Peaks: 1 = sulfuric acid, 2 = formic acid, 3 = acetic acid, 4 = propionic acid, 5 = butyric acid, 6 = valeric acid. Column: TSK SCX (5 μm), H^+ form, 20 cm × 8 mm. A 100-μl sample and a flow-rate of 1 ml/min are used.

a small amount of an acid is usually added to the eluent to keep the acidic sample compounds in the molecular form. A variety of detectors can be employed.

Tanaka and Fritz[20] separated several acids on a cation-exchange column by IEC. (See Fig. 3). The eluent was 0.5 m*M* benzoic acid in water–acetonitrile (95:5). A conductivity detector was used.

Carbonic acid and/or carbonate salts can be quickly separated and determined on a H^+-form cation-exchange column using only pure water as the eluent[21]. The H^+-form cation-exchange separation column converts carbonates and bicarbonates to carbonic acid. It also converts other salts of weak acids to the corresponding acid. Strong acids are highly ionized and pass quickly through the column. However, carbonic acid exists primarily in the molecular form and partitions between the aqueous eluent and the water inside the ion-exchange resin. A nicely separated carbonic acid peak is obtained with a retention time of about 4.5 min.

Carbonic acid is a weak acid with $pK_1 = 6.4$ and therefore is only slightly ionized. In dilute solution the ionization of weak acids increases. With carbonic acid a conductivity detector can be used; a slightly curved calibration curve is obtained between 0.05 and 5.0 m*M* solutions.

The conductimetric detection of carbonic acid can be enhanced significantly by placing a short K^+-form cation-exchange column between the separation column and the detector. This column converts the weakly ionized carbonic acid almost quantitatively to highly ionized potassium hydrogencarbonate. Further enhancement of the detector signal is obtained by placing a second OH^--form anion-exchange column just after the first enhancement column. With both enhancement columns the signal for the carbonic acid peak is increased approximately 10-fold and the calibration curve is linear over a longer concentration range.

Stevens *et al.*.[22] have recently shown that the water content of various organic chemicals can be quickly determined by ion-exclusion chromatography. Again, the separation column contains a cation-exchange column in the hydrogen form. The

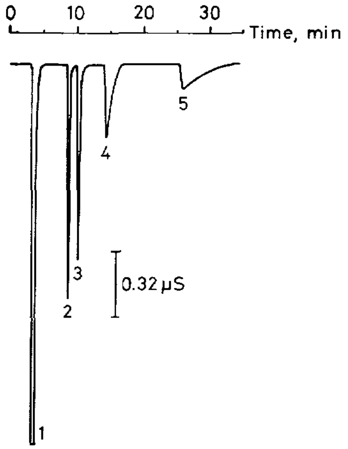

Fig. 4. Ion-exclusion separation of alcohols using an eluent of 5 m*M* aqueous sulfuric acid and conductivity detection. Peaks: 1 = void volume dip, 2 = methanol, 3 = ethanol, 4 = propanol, 5 = butanol. Column: TSK SCX (5 μM), 20 × 0.75 cm. The sample (100 μl injected) contains 0.5% of each alcohol.

eluent is dry methanol that contains a low concentration of sulfuric acid. A conductivity detector registers a change in signal when the water peak passes through the detector cell.

Tanaka and Fritz[23] separated alcohols, sugars, carboxylic acids and other hydrophilic organic compounds on a H^+-form cation-exchange resin using a dilute aqueous solution of sulfuric acid as the eluent. Using a conductivity detector, carboxylic acids give positive chromatographic peaks and non-acidic organic compounds give negative peaks (decreasing conductance). A separation of several alcohols is shown in Fig. 4.

SEPARATION OF METAL CHELATES

A broad definition of ion chromatography could include the determination of metal cations by complexation and subsequent separation of the metal complexes on a conventional LC column. This can be a very attractive approach to the analysis of metal ions. For example, Palmieri and Fritz[24] achieved a baseline separation of iron(III), hafnium(IV) and zirconium(IV) by complexing with N-methylfurohydroxamic acid and separating the complexes on a polymeric LC column.

CONCLUSIONS

During the last 10–12 years, ion chromatography has progressed from a relatively slow, seldom-used technique to one that is in broad use throughout the world. The new-found ability to rapidly determine low concentrations of anions and cations, often in complex samples, has solved countless problems in applied chemical analysis. Attempting to determine anions in any but the simplest samples without using ion chromatography is now almost unthinkable. Ion chromatography increasingly is becoming recognized as a fast and attractive way to determine metal ions and hydrophillic molecular compounds.

Many of the applications of ion chromatography to practical problems have been in the areas of inorganic analysis. For some time, the analysis of organic samples by gas- and liquid chromatography has been almost routine. So why should it not also be possible to analyze inorganic samples chromatographically? Contemporary ion chromatography is proving that such analyses are indeed possible. The impact of ion chromatography on how the scientific world quantitatively determines inorganic substances is already substantial. The momentum that has been generated is almost sure to continue.

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