Journal of Chromatography, 370 (1986) 419–426
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 19 018

COLUMN POISONING BY MULTIVALENT CATIONS IN ION CHROMATOGRAPHIC ANALYSIS FOR ALKALI METALS

DENNIS R. JENKE
Travenol Laboratories, Inc., 6301 Lincoln Ave, Morton Grove, IL 60053 (U.S.A.)
(Received August 14th, 1986)

SUMMARY

Multivalent cations from the mobile phase, stainless-steel components of the chromatographic system and analyzed samples are not eluted from the analytical column under normal elution conditions used for alkali metal determinations by ion chromatography. Thus the analytical column becomes poisoned during use with the net result that performance degrades with time. Systems properties affected include retention time, resolution, plate count and peak heights while peak areas are unaffected by changing capacity until resolution is compromised. While various methods are proposed for counteracting or preventing the poisoning effect, a technique which couples a protective precolumn to scavenge mobilized metals from steel system components with systematic injection of a flush solution to remove other interfering cations represents the most cost effective option.

INTRODUCTION

Monovalent cations (Na^+, K^+, NH_4^+, organic species) are separated and quantitated by ion chromatography with columns containing low capacity resins and weak acid eluents[1–4]. The elution conditions are such that under these conditions multivalent cations are irreversably bound to the column (regardless of manufacturer or type). Thus multivalent cations present in the chromatographic system will then poison the analytical column. The net result of this column poisoning is degrading chromatographic performance as manifested in decreasing retention, efficiency and resolution but an apparent increase in peak height sensitivity. Primary sources of these multivalent species include: (1) impurities/contaminants in the mobile phase, (2) noninert components of the chromatographic system and (3) components of the sample themselves. The first source is readily circumvented through the use of high-purity reagents for mobile phase preparation. While the second source of column contaminants would readily be eliminated through the use of chemcially inert (*e.g.* Tygon, plastic) pumps, injectors, valves and tubing, such components are relatively uncommon in operating laboratories and are available from a limited number of vendors. Although stainless-steel components of chromatographic systems can potentially be passivated by exposure to more concentrated acids, it is this authors experience that such treatments are not completely effective in eliminating metal leaching during operation.

0021-9673/86/$03.50 © 1986 Elsevier Science Publishers B.V.

Since the multivalent species which commonly cause the column poisoning can be re-mobilized with either stronger acid or complexing flush solutions, column regeneration is relatively easy to accomplish. However, if column poisoning occurs relatively quickly or only small changes in performance can be tolerated in a particular application, complete regeneration of the column must be performed relatively often and becomes cost and time ineffective. It is the purpose of this study to evaluate the magnitude of the column poisoning effect and to explore methods for its elimination/alleviation.

EXPERIMENTAL

Chromatographic system

The system employed included a Perkin Elmer Series 3B pump, a Perkin Elmer LC600 autosampler, a Bio-Rad conductivity monitor, a Linear stripchart recorder, a Dionex CFS-1 fiber suppressor and a Hewlett-Packard 3357 LAS computer integrator. The columns used were all Wescan type 269-024 high-speed cation separators. Automation equipment used for column/solvent switching included Autochrom Model 201 solenoid interface and Model 401 valve module and a Linberg Enterprises Model CD4SN ChronTrol® timer/controller. The mobile phase was 5 m*M* nitric acid supplied at a flow-rate of 2 ml/min. Depending upon application, connecting tubing and sample injector loops were either 316 stainless steel or Tygon.

Chromatographic studies

While exact experimental conditions varied in terms of analyte concentration, sample size and experimental design, the general process involved continuous injection of samples into a specific apparatus; analyte retention time, peak characteristics, peak areas and height were continuously monitored. Chromatographic columns were regenerated at the beginning and end of each analysis set by flushing with 0.1 *M* nitric acid for a period of 30 min followed by re-equilibration with the mobile phase. Both sodium and potassium were used to monitor chromatographic performance; calcium was used as a model to intentionally produce column poisoning. Both nitric acid and EDTA were evaluated in terms of their ability to act as regenerants for the columns.

Reagents

Samples were prepared by several dilutions of stocks prepared from the chloride salts of Na^+, K^+ and Ca^{2+}. Acids used for mobile phase–regenerant preparation were Ultrex® grade. All salts used were reagent grade. Deionized, distilled water was obtained from a Millipore Milli-Q® cartridge system.

RESULTS AND DISCUSSION

As noted previously, the two contributors to the capacity loss mechanism include multivalent cations either leached from the stainless-steel components of the chromatographic system or contained in the samples being characterized. In order to demonstrate the magnitude of these effects, the two processes were isolated and evaluated independently. Considering the latter process, it is common for samples

analyzed for alkali metals at Travenol to contain approximately 10 μg Ca^{2+}/Mg^{2+} per injection. As shown in Fig. 1, the continued injection of a sample containing this amount of Ca^{2+} causes a five-fold increase in the rate at which Na^{+} retention time degrades as compared to a water matrix containing no Ca^{2+}. The small loss of retention which occurs with the water matrix is attributed to leaching of transition metals from the stainless-steel components of the chromatographic system. While this effect was minimized by making all component connections with Tygon tubing, the pump and injector were still steel and thus prone to leaching. It is observed in passing that knowledge of the concentration of Ca^{2+} injected and the absolute loss of retention caused as a result of the injection allows one to estimate the total capacity of the column(s) being used.

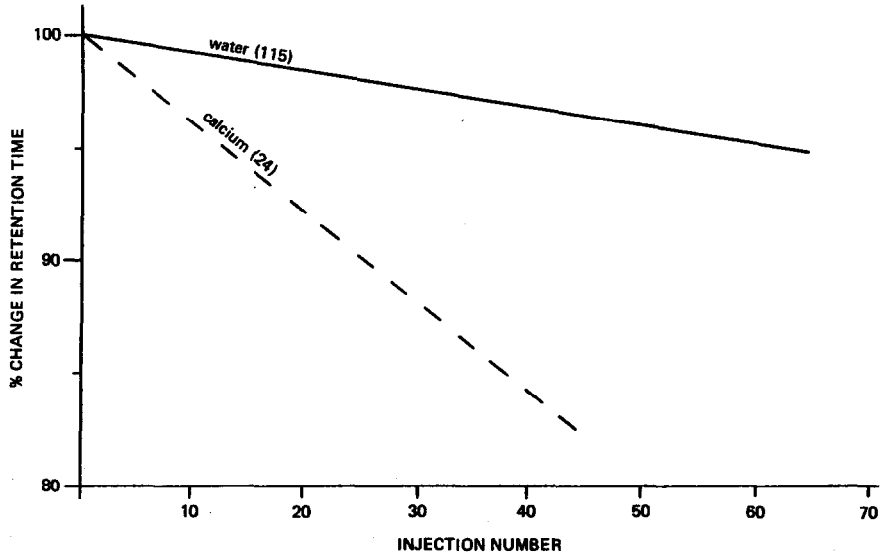

Fig. 1. Effect of sample composition on the rate of retention loss due to column poisoning. Data is for a sample using 60 ppm Na^{+} (the species being followed) in either a water matrix or one containing 40 ppm Ca^{2+}. A chromatographic system with inert tubing was used in this study. The number in brackets indicates the number of injections which produces a 10% loss in retention time.

Since a truly inert chromatographic system was not available to this research to provide a true baseline, it was impossible to assess experimentally the true magnitude of column poisoning by leaching of metals from a typical stainless-steel chromatographic system. However, it was possible to demonstrate the effect of stainless-steel connecting tubing (*versus* inert Tygon). As shown in Fig. 2, the presence of a minimum length of steel tubing increases the rate of column poisoning by nearly a factor of two. The column degradation observed was linearly related to mobile phase flow-rate, did not change in magnitude over the duration of the experiment (indicating no long term passivation is occuring) and was reproducible from column to column.

At this point in the discussion it is appropriate to note that neither type of

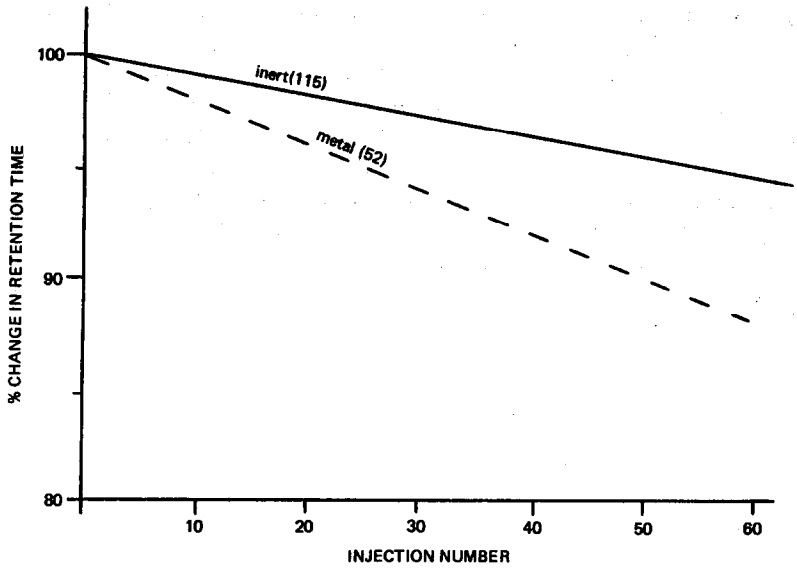

Fig. 2. Effect of the composition of connecting tubing on the rate of retention time loss due to column poisoning. Sample is 60 ppm Na^+ in water. Numbers in brackets indicate the number of injections which produces a 10% loss in retention time.

poisoning is truly irreversible in that both alkaline earth and transition metals can be removed from the column by use of a "stronger" eluent (flush). Appropriate flush solutions might include higher concentration acid (*e.g.* 0.1 *M* nitric acid) or a complexing mobile phase (*e.g.* EDTA). In some applications, the simplest way to deal with the retention loss is to ignore it (since the absolute change per sample is relatively small) and regenerate the column after a given number of injections has been made. Regeneration is accomplised by rinsing the column with one of the flush solutions mentioned above. This approach is appropriate if resolution is not critical, if only a small number of samples are to be analyzed or if peak areas are to be used for quantitation. Most pharmaceutical applications do not conform to these criteria and therefore alternative methods of eliminating/alleviating the problem were examined.

Considering the two loss mechanism separately, it is clear that three ways are potentially applicable for eliminating retention loss caused by multivalent species present in the sample. One approach would be to pretreat the sample prior to analysis (for example by selective extraction and/or precipitation). However, this approach is not time and cost effective and one must be concerned with quantitativeness as well. The latter two approaches fall under the category of column cleaning and differ with respect to quantitation of the column poisoning agent. In one scenario, the column is flushed with a higher concentration mobile phase for the sole purpose of metal removal while in the other (gradient elution) the change in mobile phase composition is such that the poisoning species can be quantitated along with the analyte(s). While in concept both approaches are sound, in practice their need for specialized equipement (gradient controllers, detectors which do not respond to the changing mobile phase) and increased per sample analysis time severly limits their utility.

Focusing on the other source of poisoning, clearly the most effective way to prevent leaching of contaminants from the chromatographic system is for the system to be completely inert. While such a system is now commerically available, it is not currently in exclusive use in cation chromatography. Thus a pertinent question raised in this research is how can one make a conventional stainless-steel system appear to be inert. Obviously, the use of PTFE or plastic connecting tubing represents an important step in this direction; however, as documented earlier, stainless-steel pump and injector components still contribute to column degradation. It is particularly difficult to isolate contaminants from the injector since to do so would require intervention after sample introduction. The intervention must be such that analytical performance is not adversely affected; an appropriate mechanism to accomplish this could not be identified by this researcher. Two aproaches which were examined both deal with pump related effects but differ in their ability to control the injector problem. In one approach, shown in Fig. 3, a pre-column containing a high-capacity cation exchange resin is placed between the pump and injector and serves to scavenge metals leached from the pump. In this study, the column contained a Dowex resin which had been hand-packed into an inert shell. Such a configuration contributes little or no back pressure to the system, cannot effect chromatographic performance, and is capable of effective column protection for long periods of use. This approach has the additional advantages of low cost and instrumental simplicty. The second approach, shown in Fig. 4, also utilizes a pre-column but in this case the column and sample injector can be switched either in or out of the analytical system. For "normal" operation, the pre-column is switched in-line and effectively protects the analytical column as the sample is being chromatographed. During sample introduction, the injector is switched in-line with the net result that the column is essentially unprotected. However, since the introduction process is only a small fraction (0.5% or less) of the total analysis time, column poisoning is minimized. While both these approaches result in a system which is virtually immune from metal poisoning (Fig. 5), the latter approach is instrumentally more complex and is not suggested for routine applications.

From this discussion, it is apparent that in order to deal effectively with both sources of column poisoning one would need to adopt a methodology that uses both protection and sequential flushing. An optimally protected system would thus include inert connecting tubing, a scavenging pre-column between the pump and injector and

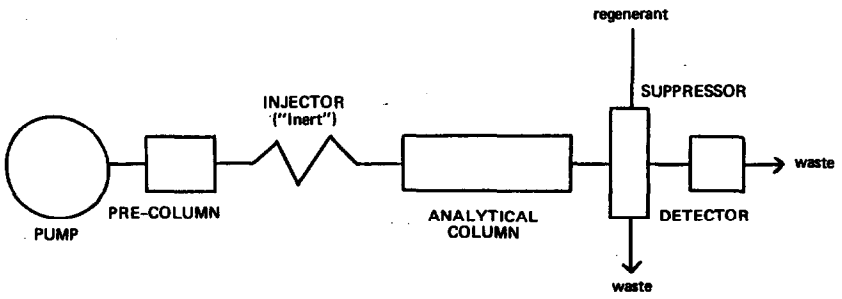

Fig. 3. Schematic diagram of the chromatographic system in which inertness is achieved by use of a scavenging pre-column.

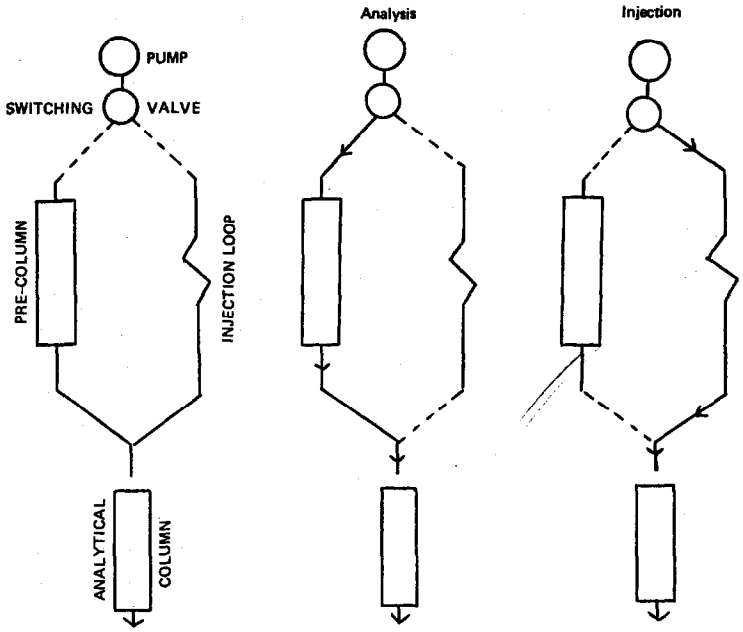

Fig. 4. Schematic diagram showing the approximation of an inert system obtained by switching between a pre-column scavenger and a sample injector.

injection of a flush solution (*e.g.* 0.1 *N* EDTA) at various points during the analytical run (say after every 30 injections of a sample). Thus one can envision a scenario in which the analyst performs a series of sequences which involves 30 sample injections

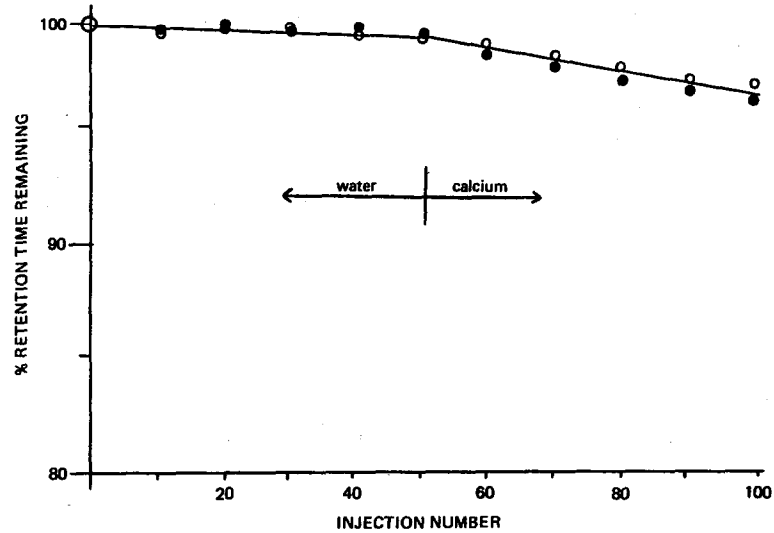

Fig. 5. Performance of both chromatographic systems shown in Figs. 3 and 4. Samples injected contained 200 ppm Na^+ (the species followed) and either water or 40 ppm Ca^{2+} as the matrix. ○ = data from system in Fig. 3; ● = data from system in Fig. 4.

TABLE I

LONG TERM STABILITY OF THE CHROMATOGRAPHIC SYSTEM: ACCURACY

Concentration injected (ppm)	*Actual concentration (ppm)*				
	Flush sequence				
	1	*2*	*3*	*4*	*5*
Sodium					
30	29.5	29.1	30.0	29.5	29.6
70	69.3	69.3	70.5	70.6	69.9
100	98.6	100.7	99.3	100.1	99.6
Potassium					
30	29.1	30.6	30.5	30.0	29.9
70	70.2	70.8	71.3	71.3	70.8
100	101.1	101.9	101.8	101.6	101.5

followed by a duplicate injection of the flush solution and a single injection of mobile phase (to allow total elution of the Na^+ from the EDTA flush) and then repeats this process as often as is necessary to complete his job. In order for this to be an effective strategy, an extremely small change in retention characteristics should be observed over the course of the run, no significant change in response should occur and no intra-sequence bias should exist. In an attempt to address these issues, samples containing 30–100 ppm Na^+ and K^+ in a matrix which was water (standards) or 20 ppm Ca^{2+} (simulated product) were repetitivily analyzed in an extended run which lasted over 27 h and involved 5 flush sequences. Results of the quantitation of samples against standards for each of the five flush sequences are shown in Table I; results obtained in every sequence are statistically equivalent at the 95% confidence level. As shown in Table II, the net change in retention observed over the course of the experiment, which consisted of over 150 injections, was extremely small. Both Na^+ and K^+ retention times changed at a rate of -0.12% per hour. While the peak height response change observed over the course of the experiment was relatively large at nearly 4%, peak area response was statistically equivalent over the entire course of the run and no trend in response was observed.

TABLE II

LONG TERM STABILITY OF THE CHROMATOGRAPHIC SYSTEM: RETENTION

Elapsed time (h:min)	*Retention time (min)*	
	Sodium	*Potassium*
0:00	4.19	8.96
7:05	4.12	8.83
15:08	4.19	9.08
24:03	4.07	8.69
27:10	4.06	8.65

CONCLUSION

Under conditions used to quantitate alkali metals, ion chromatography columns can be poisoned by multivalent cations contained in the samples themselves or leached from the stainless-steel components of conventional chromatographic systems. Utilization of a scavenging pre-column containing a high-capacity cation exchanger placed between the pump and injector coupled with sequential column flushes by injection of EDTA-containing solutions represents an effective solution to the long term degradation in column performance which results from the poisoning process.

REFERENCES

1 C. A. Pohl and E. L. Johnson, *J. Chromatogr. Sci.*, 18 (1980) 442.
2 J. S. Fritz, *LC, Liq. Chromatogr. HPLC Mag.*, 2 (1984) 446.
3 J. R. Benson, *Am. Lab. (Fairfield, Conn.)*, 17 (6) (1985) 30.
4 R. A. Wetzel, C. A. Pohl, J. M. Riviello and J. C. Mac Donald, *Chem. Anal. (N.Y.)*, 78 (1985) 355.