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# Liquid chromatography–flame ionisation detection using a nebuliser/spray chamber interface. Part 1. Design and testing

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## ARTICLE INFO

## ABSTRACT

A nebuliser and spray chamber have been used to link a flow injection analyser to a flame ionisation detector, with the potential for the combination to be used as a universal detector for liquid chromatography. The hydrogen and air flows were adjusted to achieve a stable system. The detector responded to both volatile and involatile analytes and to compounds with and without chromophores, including alkanes, alkanols, aromatic amides and acids, phenols, amino-acids and carbohydrates and gave a linear response for many analytes. However, for involatile polar analytes it was necessary to add traces of acid or salt to the carrier stream to obtain a linear response.

## 1. Introduction

Ever since the earliest days of HPLC there has been a search for a "universal" detector that could mirror the general applicability found for the flame ionisation detector (FID) in gas chromatography. The need for a chromophore limits the applicability of UV and fluorescence spectroscopic detection in liquid chromatography and the relatively low sensitivity has meant that refractometry has not proved popular, except for preparative separations. The mass spectrometer is increasingly used but still has a differential response depending on the functional groups on the analyte and the mode of operation, and for many laboratories is still too expensive for routine applications. Although the light scattering detector has been available for involatile analytes for many years [1,2] and is steadily being developed, it still has inherent problems of the loss of volatile analytes [3] and the linearity of the response [4,5]. The more recently developed corona charged aerosol detector [6,7] faces some of the same difficulties.

There have been a number of previous attempts to introduce the FID for liquid chromatography, however, the significant organic component of most mobile phases gives a high background signal. To overcome this problem a number of transport interfaces were proposed [8], which were designed to remove the mobile phase before the analyte reached the flame; by evaporation from a moving wire (which was successfully employed for lipid assays in the food industry [9]), a chain, a polymer belt, a rotating ceramic disc [10], or a titanium tape [11]. Closely related systems, principally for polymeric samples, pyrolysed the sample after desolvation and converted the products to methane before the FID [12]. However, most have not proved to be viable, although some were also investigated as early interfaces for LC–MS. The principal problems with transport interfaces were incomplete or irregular coating of the transport medium with the eluent, resulting in low sensitivity and background noise, and carry-over in recycling systems, such as the moving disc. Because they were based on the preferential evaporation of the eluent compared to the analyte they were primarily applicable to high molecular weight or involatile analytes, such as carbohydrates or lipids and as with the evaporative detectors volatile analytes could be lost.

With the introduction of superheated water chromatography (SHWC) in which the mobile phase contains no organic solvent [13–19], it was recognised that the eluent could be directly compatible with the FID. About the same time there was also more interest in the general application of high-temperature LC and the relative responses and selectivities of universal detectors for micro-column high temperature LC has been recently compared by Hazotte et al. [20,21].

In the earliest study of SHWC, Guillemin et al. [22] used the FID for the determination of phenols, sugars and iprodidione in "thermal aqueous liquid chromatography" on a 1 mm column. However, this paper contained no experimental details on the interfacing although they noted preliminary work by Wise et al. on the flame aerosol detector [23]. Subsequently, a number of groups have reported the linkage of superheated water separations

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directly to a FID by using a heated capillary. The capillary provided both a restrictor to maintain the column back-pressure and an evaporation jet, which was typically heated to 300–400 °C to generate the thermospray to carry the analyte to the flame. In an early study, Miller and Hawthorne [24] reported the detection of alkanols, amino acids and phenols showing that both volatile, and involatile analytes could be detected. Preliminary studies from this laboratory reported the separation and detection of phenols and pharmaceuticals on Hypercarb and PS-DVB columns [25] and of the homologous parabens on a polystyrene column [26]. The application of the FID was further investigated by Ingelse et al. [27] who reported a similar sensitivity to the RI detector for alkanols and alkanals but reported some problems with the blocking of capillaries and that the use of additives increased the background signal. To minimise the load of water entering the column Hooijschuur et al. [28] used an inverted FID linked to a 100 μm capillary column through an eluent jet interface and this study was subsequently extended to coupling to flame photometric detection for the detection of alkylphosphonic acids [29] and to other detectors. Wu et al. [30] examined solvating gas chromatography using a 250 μm PBD-zirconia packed capillary columns with a direct capillary interface for the separation of phenols but with no restrictor at the column outlet. A limited eluent flow was also achieved by Causon et al. [31], who used a monolithic PS-DVB capillary column and a direct linkage to the FID for the determination of the alkanols.

As an alternative, Yang et al. [32] split the effluent from a conventional 2 or 4 mm I.D. column so that only 5–11% of a column flow rate of up to 1.24 mL min$^{-1}$ reached the FID capillary. They reported quantitative results for carbohydrates, carboxylic and amino acids. They subsequently [33] examined the use of a microbore column with FID detection for the determination of amino-acids, phenols and carbohydrates and reported good linear responses and high sensitivity. Split flows and direct capillary–FID were also used by Fu et al. [34] for the separation of alkanols and aliphatic carboxylic acids. After splitting the eluent flow, Shen et al. [35] used a flow restrictor consisting of metal beads sintered into the detector to determine substituted anilines and a similar system was employed by Clark et al. [36].

The application of a superheated water–FID interface for the determination of alkanols in alcoholic beverages was examined by Yarita et al. [37] and Nakajima et al. [38]. Guillarme et al. [39] also carried out a detailed study of the alkanols and concluded that the sensitivity was comparable to GC–FID as long as the water flow rate was limited. They also reviewed [40] the different detectors including the FID that have been used with high temperature liquid chromatography. Finell et al. [41] found that for phenols short wavelength UV detection was more sensitive than the FID.

However, few of these reports seem to have been followed up by their authors into further work. A number of these studies noted problems with blocking of the capillary when involatile analytes, such as carbohydrates, were being examined and similar difficulties were noted in our preliminary studies. Within a directly linked SHW–FID system the capillary performs two functions; firstly to maintain a sufficiently high back pressure in the column so that the mobile phase in the column remained in the liquid state at elevated temperature, and secondly to present the sample to the flame by flash evaporation, and it appears that these two operations may conflict as high temperature evaporation causes deposition of the analyte in the narrow capillary tube from the column.

The present work describes an alternative interface which separates the two functions, in which an unheated restrictor is followed by low temperature nebulisation to provide the analyte in an aerosol which enters the flame. This was expected to provide a milder technique avoiding high temperature evaporation. The development of this work has led to a patent application [42]. The
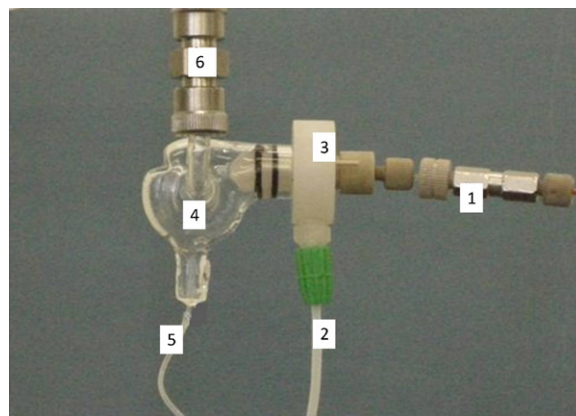


**Fig. 1.** Nebuliser/spray chamber assembly: (1) carrier flow, (2) nebulising gas, (3) nebuliser, (4) spray chamber, (5) condensate to drain, (6) connection to detector base.

design of the interface, the conditions needed to maintain the flame and the linearity of the responses will be investigated for a series of potential analytes using a flow injection carrier stream. The application to HPLC separations and the relative responses of the detector for analytes containing different functional groups, and comparisons with other detectors, will be reported in the following paper [43].

## 2. Experimental

### 2.1. Materials

Maltose, valine, decyl alcohol, ethylene glycol, poly(ethylene glycol), glycerol, 4-hydroxybenzamide, 4-hydroxybenzoic acid, methanol, propanol, and resorcinol were obtained from Aldrich Chemical Co., Poole, Dorset, UK. Dichloromethane, hexane, ammonium sulphate, sodium sulphate and sulphuric acid, hydrochloric acid, orthophosphoric acid and nitric acid were from Fisher Scientific, Loughborough, England.

Air, hydrogen and nitrogen were from BOC gases Worsley, Manchester. De-ionised water was prepared in the laboratory with an ELGA (High Wycombe, England) water purification system.

All samples were prepared as solutions in de-ionised water.

### 2.2. Instrumentation

The FIA–FID was assembled using a Hewlett Packard 1050 quaternary pump (Waldbronn, Germany), attached to a dummy packed LC column to provide a back-pressure to the pump to stabilise the flow rate. A Rheodyne 7125 injector 10 μL (Cotati, CA), valve was connected to a Cetac micro-concentric nebuliser (MCN-100) (Omaha, NE), in which the glass nebuliser capillary had been replaced with a 0.009 in. ID stainless steel capillary (Coopers Needle Works, Birmingham, West Midlands, UK). The spray was fed into a 40 mm ID centrifugal spray chamber with a dimple [44]. Any condensed eluent was removed from the spray chamber using a Gilson M313 peristaltic pump (Villiers le Bel, France) (Fig. 1). The nebuliser and spray chamber were placed in an isothermal oven at 40 °C. The aerosol was passed through a 1/4 in OD glass tube to a slightly modified flame ionisation detector from a 3300 Varian gas chromatograph (Walnut, CA), which was controlled by the 3300 GC electronics. The standard jet of the FID was replaced with a metal tipped 33 mm × 2 mm ID ceramic tube to permit a higher gas flow and the detector was set at 230 °C to prevent condensation. The signal from the detector was recorded using Clarity software (DataApex, Prague, Czech Republic) and limits of detection were

calculated as the mass of sample, which gave a signal 3 times the noise level.

The standard operating conditions of the FIA–FID were: carrier flow, $1\,mL\,min^{-1}$; nitrogen nebuliser gas, $250\,mL\,min^{-1}$; FID hydrogen flow, $157\,mL\,min^{-1}$ and air flow, $650\,mL\,min^{-1}$.

## 3. Results and discussion

### 3.1. Direct capillary interface

In preliminary studies, we examined the application of a heated glass capillary or crimped metal capillary as potential interfaces. As with earlier researchers, it was found that the response of the detector was sensitive to the position of the tip of the capillary below the jet of the FID. The temperature of the FID heater block was also critical and needed to be at 350–400 °C to cause rapid volatilisation and a fine thermospray into the flame. To overcome the cooling effect of the water vapour, the flow rate was limited to $0.16\,mL\,min^{-1}$ and the hydrogen and air flows had to be increased to 600 and $250\,mL\,min^{-1}$, respectively, considerably higher than for use with a GC. To accommodate these high gas flows the standard analytical jet in the FID was replaced with a metal-tipped ceramic jet with a 2 mm internal diameter. Similar high temperatures and hydrogen and air rich flames were also used by other researchers to achieve stability. Increasing the flow rate of the water or reducing the hydrogen flow usually caused the flame to be extinguished or become unstable. As the intention in the present study was to use conventional columns of 3 mm or 4.6 mm I.D. for LC, it was desired to able to accept an eluent flow rate of up to $1\,mL\,min^{-1}$.

Although the heated capillary interface worked well for some analytes, such as the alcohols and parabens [26], when it was examined in the current study it lacked robustness and the capillary tube was prone to blocking particularly with involatile analytes, such as carbohydrates. Similar problems were also noted by Ingelse et al. [27]. The initial part of the present study therefore examined in more detail the configuration and heating methods of the capillary. The primary interest in this detector is its potential to detect involatile analytes that cannot be analysed by gas chromatography and for which the UV spectroscopic detection is unsuitable. Using a direct injection system with no column, it was possible to detect a number of carbohydrates in aqueous solution. However, there were frequently problems with blocking of the capillary and it appeared that during the evaporation of the aqueous solution, the residual carbohydrates were charring and the residue was coating and eventually blocking the capillary. Similar problems occurred with other involatile analytes, such as the amino-acids. Because it seemed that the problem was during the evaporation stage, a series of modifications were carried out to alter the way in which the hydrogen flow was introduced around the capillary and the temperature needed to maintain the spraying process. However, although short term improvements were sometimes found none of the designs or operational combinations was stable and robust for a reasonable period. Although other groups have used this approach, especially for more volatile analytes such as the alkanols, these problems may explain why further work has not usually been reported. It was concluded that the problem was because the capillary has two conflicting roles. It has to be relatively narrow to provide a back-pressure restriction to the superheated water in the chromatographic column to prevent the mobile phase from boiling. It also has to be held at a high temperature to generate the thermospray needed to carry the analytes into the flame. This was causing no problems with volatile analytes but less volatile analytes were decomposed at 300–400 °C or dissolved silica from the column was leaving involatile residues. A wider capillary would not block as easily but would not control the column pressure and the eluent

could boil inside the column during a superheated water separation.

It was therefore decided to separate these two roles. A restrictor would be placed at the end of the column, which would form a low temperature condensed eluent flow and a nebuliser would then be used to generate an aerosol, which would carry the analyte into the flame. Neither stage would have to be at a high temperature thereby eliminating the charring effect. Nebulisers are well known in a number of areas in particular as interfaces for liquid samples in atomic absorption or inductively coupled plasma spectrometry [45] and are often coupled with spray chambers to remove large droplets and reduce signal noise. In the present study a standard commercial nebuliser was employed, but to accommodate the higher eluent flows typical of LC, the silica capillary was replaced with a 0.009 in. ID stainless steel capillary. It was connected to a centrifugal spray chamber, based on a design which has been previously used in this laboratory as a CE-ICP–MS interface [44], which included a dimple to disrupt the gas flow and enhance the wash-out performance. The purpose of the spray chamber was to remove the larger droplets that might cause detector noise but this meant that part of the carrier flow (and sample) would be lost. The spray chamber was thermostated at 40 °C to prevent condensation.

Solutions of valine were injected using a FIA system to determine the effects of the operating parameters. Based on preliminary trials, the initial conditions were: carrier flow rate, $1\,mL\,min^{-1}$; hydrogen flow, $157\,mL\,min^{-1}$; air flow, $650\,mL\,min^{-1}$; nebuliser nitrogen flow, $184\,mL\,min^{-1}$; spray chamber internal diameter, 30 mm. The peak areas increased as the carrier water flow rate decreased from $1.5\,mL\,min^{-1}$ (395 mV s) to $1.0\,mL\,min^{-1}$ (412 mV s) to a maximum at $0.5\,mL\,min^{-1}$ (630 mV s), however, at this flow the peak was noisy and $1.0\,mL\,min^{-1}$ was chosen for the rest of the study. Although these changes could be the result of changes in the efficiency of the nebulisation, they could also suggest that the detector may be to some extent dependent on the proportion of the vapourised water in the eluent gas stream but this would need to be confirmed in further studies The hydrogen flow was tested from 76 to $332\,mL\,min^{-1}$ and gave the maximum signal at $157\,mL\,min^{-1}$. The response was relatively insensitive to the air flow above $500\,mL\,min^{-1}$ and $650\,mL\,min^{-1}$ was chosen for the study. Other groups used similarly high hydrogen flow rates with the water–FID, for example Miller and Hawthorne [24] employed $300\,mL\,min^{-1}$ of hydrogen and $430\,mL\,min^{-1}$ of air with a water eluent flow of $200\,\mu L\,min^{-1}$ and Yang et al. [32] with the limited water flow from their capillary column used $135\,mL\,min^{-1}$ of hydrogen and $360\,mL\,min^{-1}$ of air and typically used detector temperatures of 350–400 °C.

Changing nitrogen flow rates to the nebuliser from 125 to $353\,mL\,min^{-1}$ suggested an optimum flow of $250\,mL\,min^{-1}$. Increasing the diameter of the spray chamber from 30 to 40 mm increased the signal and this diameter was used throughout the remainder of the study. Because of non-linear responses from the detector for some analytes (see later) the effect of the potential across the detector and the dimensions of the collector were examined. However, changing the voltage from 200–400 V had no effect on the linearity and little change in the overall response. Increasing the internal diameter of the collector from 4 to 6 mm or altering the length to increase the surface area produced little change in signal intensity. The internal diameter of the FID collector therefore was left at 4 mm and the potential at 170 V.

Although in GC the FID is normally regarded as being a nearly universal detector it can respond significantly differently to different analytes [46,47]. Generally the presence of a hetero atom will reduce the relative response and the early members of the oxygenated homologous series, such as formic acid, formaldehyde and methanol, typically give weak signals. The presence of a high proportion of water in the carrier flow and the different combustion
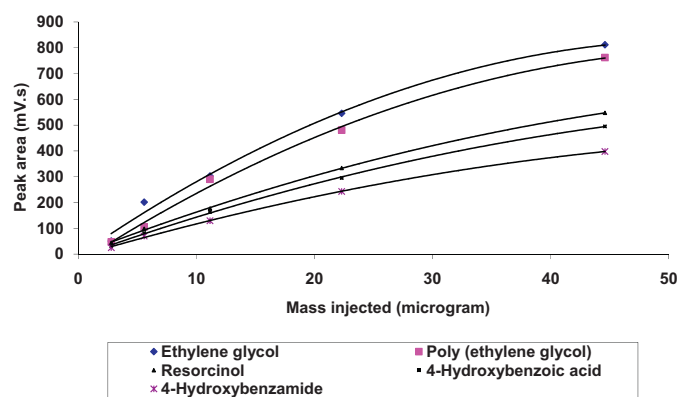
**Fig. 2.** Response of the FID to non-volatile analytes. FID conditions as in Section 2.



**Fig. 3.** Effect of carrier pH on response of valine. FID conditions as in Section 2. Carrier liquid: 0.0007 M sulphuric acid (corresponding to pH 3), 0.0007 M ammonia solution (corresponding to pH 9) and water.



**Fig. 4.** Effect of carrier water additives on the FID response of valine. FID conditions as in Section 2.

gas proportions and temperatures might also alter the responses in FIA–FID, compared to GC–FID, so a range of model analytes were investigated and the relative signal strengths and the linearity of their responses were determined.

Aqueous samples of methanol (18.5 μg–0.07 μg), propanol (21.4 μg–0.08 μg), hexane (80 μg–5.0 μg) and dichloromethane (46.8 μg–2.93 μg), were introduced into the detector. All gave linear responses ($R^2$ from 0.948 to 0.999) and had intercepts near zero. Similar correlations were obtained in the previous studies of the alkanols and the results had been used for quantitative assays [24,37]. As expected from gas chromatography, the response of propanol, was significantly higher than methanol. Surprisingly, hexane gave a low response and unexpectedly dichloromethane responded strongly although it usually responds only weakly in GC. These results might suggest that the mechanism of the ionisation process in the aqueous FID flame differs from the gaseous system. A more detailed comparison of a wider range of different chemical groups is explored in more detail in the LC–FID mode in the following paper [43].

A number of more polar analytes, which would often be too involatile for GC, were then injected: maltose and valine both gave a linear response from 20 to 160 μg but deviated at lower levels down to 1.25 μg. In contrast, Yang et al. [33] using a capillary column–FID, reported a linear response from 6 to 6000 ng. However, in the present study the responses for ethylene glycol (2.78 μg–22.2 μg), poly ethylene glycol (2.04 μg–16.3 μg), resorcinol (2.25 μg–18.0 μg), 4-hydroxybenzoic acid (1.65 μg–13.2 μg), and 4-hydroxybenzamide (1.63 μg–13.0 μg), were non-linear (Fig. 2) and the signals appeared to become saturated at higher masses.

Because the pH of the carrier stream might affect the ionisation in the flame, low levels of acids and bases were added to the carrier water. When dilute 0.0007 M ammonia solution (corresponding to pH 9) or pure water was used as the carrier the analytes gave non-linear responses (see valine, Fig. 3). However, a dilute solution of 0.0007 M sulphuric acid (corresponding to pH 3) as the carrier gave linear response curves, but the magnitudes of the signals were reduced (compared to those shown in Fig. 2). The response for valine was linear over a wider range ($R^2$ = 0.9999), from 1.25 to 160 μg. Similar results were obtained for a non-ionisable solid, maltose ($R^2$ = 0.9995), and two low volatility liquid samples (decanol and glycerol). However, two volatile analytes, *m*-cresol and benzyl alcohol, gave linear results in both water and dilute acid although the signal was reduced in the acid carrier.

Valine (2.5–20 μg) was then examined using carrier solutions containing traces of either hydrochloric, nitric or orthophosphoric acids and it gave a linear response in all three cases (Fig. 4). However, orthophosphoric acid resulted in marked 10 fold increase in sensitivity but also a much high background noise signal, whereas the curves for nitric and hydrochloric acids gave significant positive
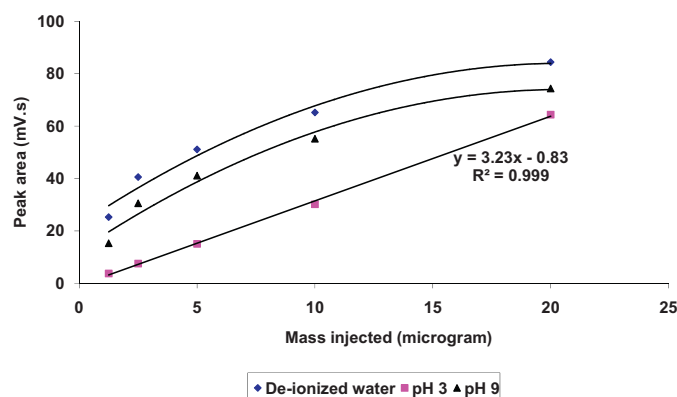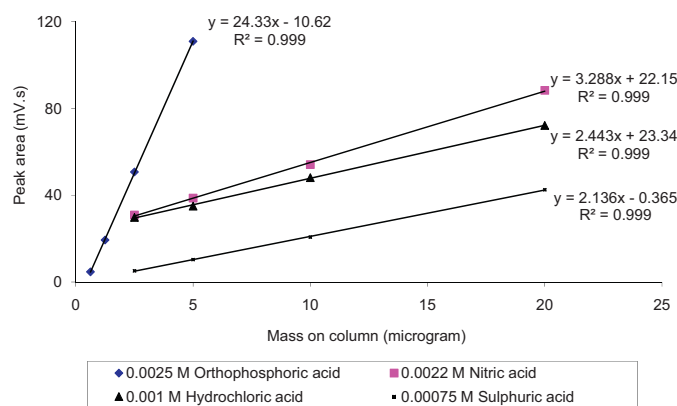
intercepts, which could be due to the acids attacking the metal tubing. Repeating the experiment with phosphoric acid in the carrier after a 24 h delay showed that the enhanced sensitivity has been lost and the background noise was reduced so there may have been pacification of active surfaces.

To minimise potential corrosion, salts of the acids were examined as additives. Injecting valine into both 0.005 M sodium sulphate ($y$ = 1.91$x$) and 0.005 M ammonium sulphate ($y$ = 1.80$x$) gave linear responses very similar to that of 0.00075 M sulphuric acid ($y$ = 2.14$x$ − 0.37). The results with ammonium sulphate after a 24 h delay showed no significant change and the signal was largely unaffected on changing the salt concentrations from 0.0025 M to 0.00025 M. The reason for these effects is unclear and may suggest a complex ionisation process in the FID flame.

Following the establishment of suitable operating conditions for the use of the nebuliser–FID detector with flow injection analysis, the following paper describes the application of the detector to monitor LC separations using room temperature or superheated water eluents for the determination of both relatively volatile aliphatic and aromatic organic compounds, and involatile polar analytes such as carboxylic and amino-acids and carbohydrates and to compare its linearity and sensitivities with UV and RI detection [43].

## 4. Conclusion

The use of a nebuliser as an interface between a flow injection system and a flame ionisation detector has been shown to be practical with adjustment of the hydrogen and airflows and can be used to

detect the presence of a range of organic compounds. The response of the more volatile and liquid analytes was linear probably because they were largely vapourised during the nebulisation stage, but the responses differed from those in GC. Involatile analytes, such as carbohydrates and amino-acids, gave non-linear response unless dilute acid or salts were added to the carrier. The detector therefore has potential to be used as a universal detector with HPLC when water or superheated water is being used as an eluent.

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