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Review

Gas chromatographic detectors for use in column liquid chromatography

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ABSTRACT

Gas chromatographic detectors are increasingly used in order to obtain sensitive and selective detection in both conventional-size and miniaturized column liquid chromatography. A critical review of the literature is given, with suitable emphasis on instrumental design, optimization of interfaces and applications. Future trends are discussed.

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1. INTRODUCTION

In recent years, continuing research in instrumental chromatographic techniques has led to many interesting developments in capillary gas chromatography (GC) and column liquid chromatography (LC). With the introduction of supercritical fluid chromatography (SFC), three sophisticated complementary separation techniques are now available for the analytical chemist who, today, is increasingly faced with complex trace-level analyses in the fields of environmental, industrial and biomedical chemistry. With the complex samples often under investigation, extensive off-line or on-line sample clean-up and/or trace enrichment are generally necessary. To simplify these sometimes complicated and time-consuming procedures, a more direct approach using a highly sensitive and selective detector system is often desirable. Good examples of selective and sensitive detection in trace analysis, illustrating an approach that does not require extensive sample clean-up, are mentioned by Hutte *et al.* [1] in a review on the development of chemiluminescence detection for GC. Generally, detection is a strong point of GC, where sensitive and selective detectors such as those for electron-capture (ECD), flame photometric (FPD), thermionic (TID) and nitrogen–phosphorus (NPD) detection are commercially available.

Today, LC with its wide range of separation procedures is the most versatile chromatographic technique. With the use of normal-phase, reversed-phase, ion-pair, ion-exchange or gel-permeation LC, a separation can be achieved for almost any class of compounds. With the introduction of miniaturized LC, *i.e.*, the use of microbore (0.5–1 mm I.D.), micro (0.1–0.5 mm I.D.) and capillary (0.05–0.1 mm I.D.) columns, in the late 1970s, new detection modes became available. Recently, Novotny [2] reviewed the advantages of several types of detection systems (and their miniaturization) in microcolumn LC. Not surprisingly, the combination of the separation power of LC and the sophisticated detector systems currently being used in GC is an area of increasing interest. This paper reviews the developments in coupling LC on-line with GC detectors. Combining LC with, *e.g.*, mass spectrometry, nuclear magnetic resonance or Fourier transform infrared detectors is not covered in this survey. For comprehensive reviews in this area, the reader should consult, *e.g.*, refs. 3 and 4.

2. GAS CHROMATOGRAPHIC DETECTORS USED IN LIQUID CHROMATOGRAPHY

A survey of GC detectors compiled from information sent by the manufacturers and/or distributors of GC instrumentation was recently published in *European*

Chromatography News [5]. This survey and other reviews on GC [6–8] show that increasing numbers of GC detector types are being used today. The following types of GC detector are frequently mentioned: flame ionization, photoionization, electron-capture, flame photometric, microcoulometric, thermal conductivity, chemiluminescence, electrolytic conductivity and thermionic.

A survey of the literature, including the database of *Chemical Abstracts* up to January 1990, was performed, combining the keywords "liquid chromatography" or "LC" with the above GC detector types. In the case of GC and LC detection techniques based on similar detection principles, only gas-phase detection was included in the overview. As a result, electrolytic conductivity and microcoulometry had to be excluded, because both techniques are based on detection in an electrolyte solution after combustion or hydrogenolysis. Most papers on chemiluminescence and photoionization had to be discarded for similar reasons. Fig. 1 shows the result of the literature search.

Since the early years of LC, there has been a need for a universal mass-sensitive detector. Therefore, in the early history of coupling LC to GC detectors, *i.e.*, in the period 1968–73, most work was devoted to the use of flame ionization detection (FID), as shown in Fig. 1. Fig. 1 also shows the application of other GC detectors, such as those for chemiluminescence (CLD), electron-capture (ECD), flame photometric (FPD), thermionic (TID) and photoionization (PID) detection, which have become increasingly important in more recent years. In the past decade, many papers have been published which deal with CLD and, especially, the use of thermal energy analysis (TEA) in combination with conventional LC. The use of ECD for selective LC detection has also become popular in the past decade. PID is a rather novel detection technique in GC, which may explain why only a few papers have appeared up to now on LC–PID. Only two papers have been published on LC with thermal conductivity detection (TCD), both originating from the period 1968–71. An explanation may be that TCD, although widely applied in GC, is less suitable for coupling to LC because of the variation of its response depending on the compound and detector operating conditions. Finally, Fig. 1 demonstrates the increased use of GC detectors in miniaturized LC systems since the early 1980s.

3. INTERFACING LC TO GC DETECTORS

Interfacing LC to GC detectors or, more specifically, introducing the analytes dissolved in a liquid phase into a heated detection zone or flame is a difficult problem. Key parameters are the LC effluent flow-rate and composition, and also the type of GC detector to be interfaced. Ideally, an interface should be able to introduce all analytes into the detection zone or flame independently of their physical properties, while the GC detector should be able to accept the total LC effluent and maintain its main characteristics as a GC detector, such as linearity and sensitivity. Unfortunately, these demands have not yet been fully met in any published set-up. The present developments are interesting and promising, however, as will be shown below.

3.1. Transport systems

To solve the problems encountered when introducing a liquid mobile phase into a GC detector, LC effluent transport systems were designed based on the work of

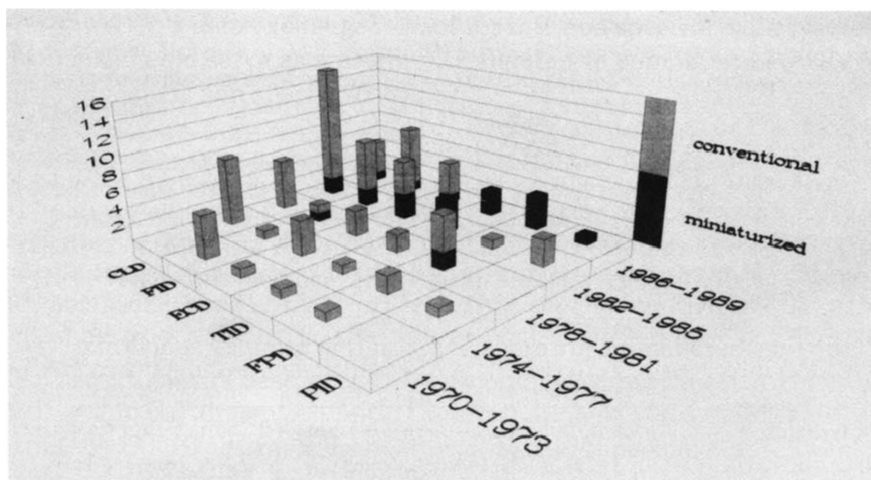


Fig. 1. Number of papers on LC systems coupled with GC detectors during the period 1970–1990.

Haahti and Nikkari [9] and James *et al.* [10]. A transport system consists of a carrier, which can be a metal chain, wire or disc, or another similar device which is continuously rotating between the LC effluent introduction point, an evaporation unit and the detector. The liquid LC effluent is loaded on the moving part of the system and, subsequently, removed by evaporation. Next, the non-volatile analytes are either brought into a pyrolysis furnace or directly into a flame, depending on the detector system used. Most transport systems are applied in FID and they will be discussed in more detail in the pertinent section below.

In 1984, Yang *et al.* [11] presented a new transport system based on thermospray vaporization coupled to a PID or an ECD instrument. A schematic diagram of their system is shown in Fig. 2. The transport device is similar to earlier systems in that a moving surface is required, the sample being detected after the solvent has been removed. The unique feature of the approach is that the sample is vaporized and the solvent removed without being deposited as a liquid on the moving surface. This is

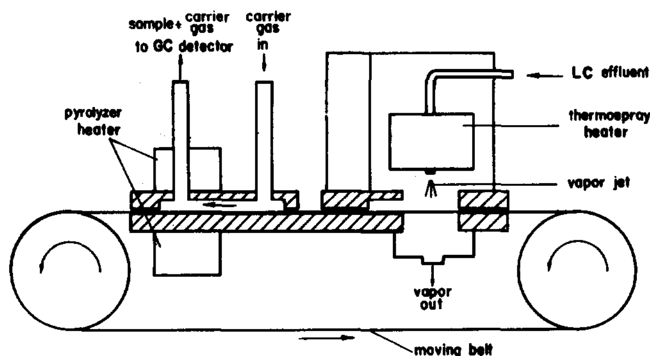


Fig. 2. Schematic diagram of LC detector employing thermospray deposition of the sample onto a moving belt and sample detection by vaporization or pyrolysis of the sample into standard GC detector [11].

accomplished by using a heated thermospray vaporizer, which creates a superheated mist carried in a supersonic jet of vapour. Non-volatile molecules are preferentially retained in the droplets of the mist. When the droplets deposit on the moving surface, which is placed perpendicular to the vapour jet, under optimized temperature and flow conditions, most of the effluent will be vaporized. The analytes are then carried into a pyrolyser chamber and, after pyrolysis, are transported into the GC detector by means of a carrier gas.

3.2. Direct introduction systems

A transport system can be considered as an indirect way of interfacing LC systems and GC detectors. With direct introduction, the analytes dissolved in the LC effluent are transported into the detection zone or flame as a liquid, for example as fine droplets or an aerosol. This approach involves the use of a nebulizer or spraying device. An example of an aerosol interface is shown in Fig. 3. Another, but less direct, way of interfacing is to use an evaporation interface. In this instance the liquid effluent is totally evaporated via a heated capillary or desolvation chamber and then introduced into the detection zone as a gas. Interfacing by direct introduction or via evaporation places special demands on the GC detector. Selective GC detectors are to be preferred in this instance. Recently, Brinkman and Maris [12] reviewed the use of selective GC detectors in LC. As regards the LC mobile phase, the relatively high flow-rates of 0.5–3 ml/min in conventional-size LC seriously limit one's choice if total introduction of the LC effluent is aimed for. Successful attempts appear to be restricted to coupling with ECD [77–89] or FPD [52–59], which will be discussed in detail below. When using reversed-phase eluents, generally only a small part of the LC effluent is introduced, which often results in seriously reduced sensitivity. On the other hand, direct interfacing of LC with GC detectors has become distinctly more popular with the advent of miniaturized LC with its flow-rates of, typically, 1–50 μl/min.

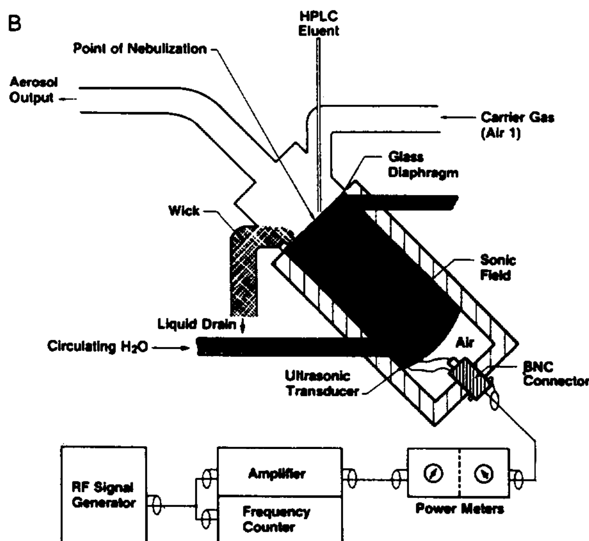


Fig. 3. Schematic diagram of the micronebulizer [62].

4. FLAME IONIZATION DETECTION

In his book on liquid chromatographic detectors, Scott [13] extensively described the development of transport systems for FID, and reported on the then commercially available Pye Unicam LCM2 system which was introduced in the late 1970s. Published applications of this and other of LC–FID systems are summarized in Table 1.

More recently, another transport FID has become available, *viz.*, the Tracor Model 945 LC–FID system, which was introduced at the 1983 Pittsburgh Conference and was described in detail by Dixon [14].

The detector (Fig. 4) consists of a fibrous quartz belt at the periphery of rotating

TABLE 1

APPLICATIONS OF TRANSPORT LC–FID SYSTEMS

Class of compounds	Detector type[a]	Ref.
Lipids	b, b, b	18, 19, 20
	e, e	35, 36
Triglycerides	b, c, b, b	27, 33, 19, 20
	b, e, f, a	21, 15, 23, 38
Sterols	c, a, b, e	27, 29, 19, 15
	e, e	14, 37
Phospholipids	c, b, e	27, 19, 15, 39
Albumin	c, b	28, 18
Hydrocarbons	e, d, e	17, 34, 16
Squalane	f, d, f	30, 31, 32
Carbohydrates	b, f, e, e	18, 24, 14, 37

[a] a = Moving wire [29]; b = moving belt [18]; c = moving chain [27]; d = rotating disc [31]; e = Tracor 945; f = Pye Unicam LCM 2.

disc enclosed in a heated-air-swept housing. The total LC column effluent is applied as a fine stream onto the rotating porous quartz belt. As the disc rotates, the solvent is vaporized while the non-volatile analytes are carried to the FID. A second, much hotter flame is used to clean the belt. Using the Tracor LC–FID system, Maxwell *et al.*

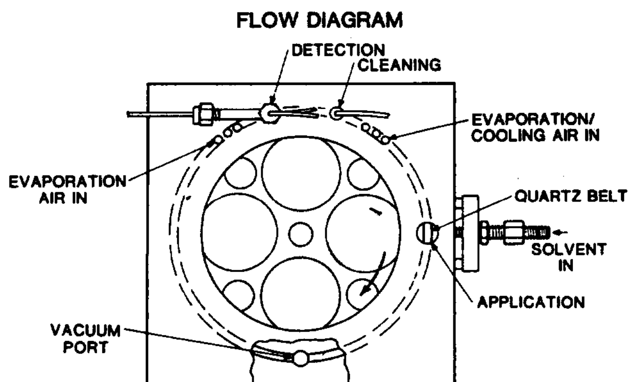


Fig. 4. Flow diagram of the Tracor LC–FID [14].

[15] performed linearity studies on sterols, glycerides and phospholipids. Each of the lipid classes gave a linear response over the tested range of 6–200 μg with correlation coefficients, *r*, of over 0.9978. By modifying the system, which allowed a reduction of the evaporation block temperature from 150 to 68°C, Pearson and Gharfeh [16,17] were able to extend the use of the system to the lower molecular weight alkanes, *i.e.*, from C_{32} to C_{24}.

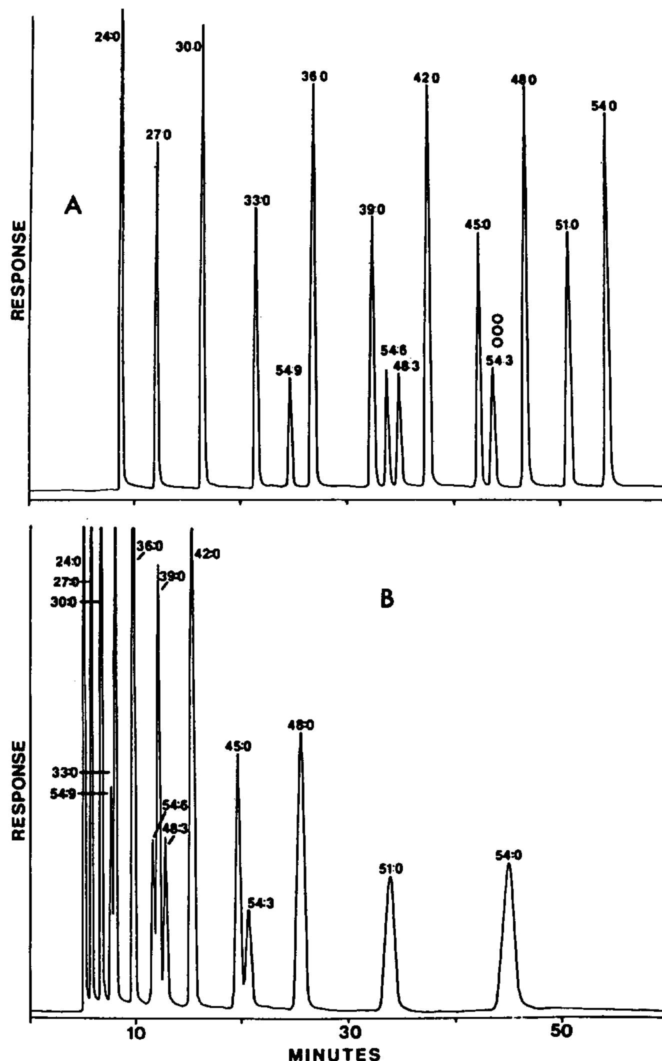


Fig. 5. Separation of triglyceride mixture HPLC G-1. Column, 250 × 4.6 mm I.D., 5 μm, Zorbax C_{18} ODS with 15% carbon content (column 1). (A) Mobile phase, 60-min linear gradient from 15 to 55% methylene chloride in acetonitrile; flow-rate, 0.8 ml/min; sample size, 40 μg; detector, flame ionization. (B) Isocratic elution with 45% methylene chloride in acetonitrile. Peaks: number before colon = number of carbon atoms in acyl chains and number after colon = number of double bonds in acyl chains: 24:0 = Tricaprylin; 27:0 = trinonanoin; 30:0 = tricaprin; 33:0 = triundecanoin; 54:9 = trilinolenin; 36:0 = trilaurin; 39:0 = tritridecanoin; 54:6 = trilinolein; 48:3 = tripalmitolein; 42:0 = trimyristin; 45:0 = tripentadecanoin; 54:3 = triolein; 48:0 = tripalmitin; 51:0 = triheptadecanoin; 54:0 = tristearin [21].

Parallel to the development of commercial LC–FID systems, Privett and Erdahl [18] improved an earlier laboratory-made LC–FID design. Their system is based on the use of a perforated stainless-steel belt for the collection and transport of the LC column effluent. After evaporation of the solvent, the analytes are converted to hydrocarbons in a stainless-steel reactor and detected by FID. Privett and co-workers used this system for the determination of albumin, glucose and lipids [19,20]. A recent application [21] to the determination of triglyceride species present in vegetable oils is shown in Fig. 5.

Recently, a different type of transport device was developed by Malcolme-Lawes and Moss [22]. It consists of a number of 1-mm diameter drawn quartz rods mounted on a two-part disc. When liquid LC effluent (under normal operating conditions *ca.* 10 μl) is deposited on a rod, the rod moves through a three-step air-flow evaporation system. After the end of the third step the rod is placed in the centre of the flame of an unmodified flame ionization detector. During the operation, the system is under computer control. First studies on normal-phase LC gave a repeatability of better than 2% for four successive injections of 10 μg of pyrene and good linearity for 1–10 μg of injected sample. For the lower molecular weight alkanes, the system can be used down to about C_{22}, which is comparable to the results of Pearson and Gharfeh [16,17]. The limit of detection for both pyrene and C_{36} alkane was of the order of 100 ng.

4.1. Miniaturized LC

The advantage of transport systems is that the volatile constituents of the LC column effluent are removed completely. The limitation is that only a small fraction of the effluent is coated onto the moving surface of the transport system. This is due to the relatively high flow-rates used in conventional LC. If, however, miniaturized LC systems are employed, the entire column effluent can be deposited on a suitable matrix for FID. Tsuda *et al.* [23] were the first to combine micro-LC with a commercially available system, *viz.*, the Pye Unicam wire-transport flame ionization detector, as shown in Fig. 6. This wire-transport detector was not modified except for the loading system, which consisted of a micro glass capillary tube (20 mm × 50 μm I.D. × 0.65 mm O.D.) inserted into the end of the LC column, which was constructed of PTFE tubing (I.D. 0.5 mm). The entire effluent of 2–12 μl/min was fed into the glass capillary and loaded onto the moving wire. A detection limit of 10–20 ng for triolein was reported but a non-linear relationship was found in the range 1–1000 ng. In 1986, Veening *et al.* [24] also reported on the use of the Pye Unicam moving-wire flame ionization detector in combination with microbore LC (1.2 mm I.D. columns). The system was compatible with the low flow-rates (60–100 μl/min) of microbore LC. For a series of carbohydrates, the limits of detection ranged from 160 ng for xylose to 400 ng for lactose. Linear calibration graphs were recorded for xylose, glucose, sucrose and maltose between 0.3 and 13 μg.

Krejci and co-workers [25,26] described a special burner designed for the on-line coupling of capillary LC columns (5–34 μm I.D.) to GC detectors, which was used for flame ionization and thermionic detectors. The burner (Fig. 7) consists of a quartz tube into which the tip of the capillary column is inserted. The temperature at the end of this column can be varied from room temperature up to *ca.* 700°C. The authors claimed an identical transfer velocity into the detector for analytes with boiling points in the range 80–320°C. The FID system can be used with mobile phases that contain methanol;

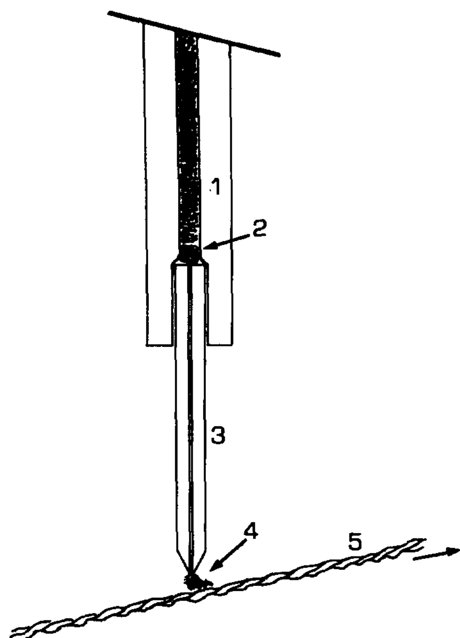


Fig. 6. Schematic diagram of total effluent loading system. 1 = Micro-column (I.D. 0.5 mm, O.D. 2 mm); 2 = quartz-wool; 3 = microglass capillary tubing (I.D. 50 μm, O.D. 0.65 mm); 4 = effluent; 5 = twisted steel wire (I.D. *ca.* 0.2 mm) consisting of three strands [23].

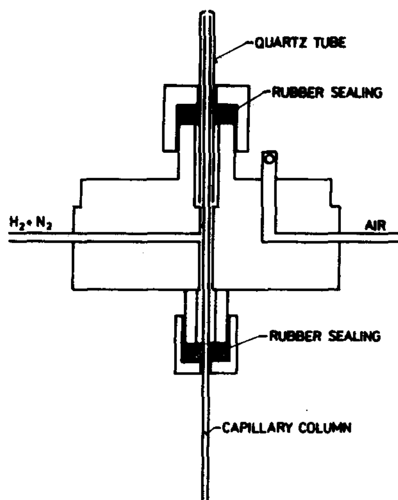


Fig. 7. Diagram of the flame ionization burner [25].

however, a decrease in response has to be accepted, depending on the methanol content. An example of a capillary LC–FID application is shown in Fig. 8. The minimum detectable mass flow-rate for the detector was 1 pg/s for *m*-cresol.

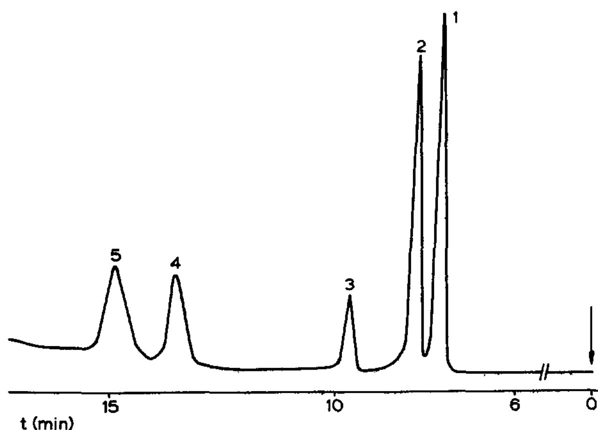


Fig. 8. Example of a chromatogram with flame ionization detection. Column, 3 m × 14 μm I.D.; stationary liquid, OV-101; mobile phase, water. Solutes: 1 = triethylene glycol; 2 = *m*-cresol; 3 = 2,4-dimethylphenol; 4 = 2 methyl-4-ethylphenol; 5 = 2-isopropylphenol [25].

5. THERMIONIC DETECTION

Thermionic detection (TID) is extensively used in gas chromatography because of the excellent sensitivity for phosphorus- and nitrogen-containing substances. For this reason the technique is also known as nitrogen-phosphorus detection (NPD).

TID/NPD was first coupled to LC in 1973 [40]. Here, as in several later instances [41–43], modified transport FID systems were used in combination with conventional-size LC set-ups. In coupling LC to GC-type detectors there has been a trend towards the miniaturization of column dimensions to reduce solvent introduction, which results in better compatibility with selective detection. On-line LC–TID is a good example to demonstrate the benefits of miniaturized LC and here all further work has been carried out with narrow-bore or even smaller columns.

5.1. Flame-based thermionic detection

In 1983, McGuffin and Novotny [44] described a dual-flame thermionic detector for on-line use with micro-LC (Fig. 9). The total microcolumn effluent was concentrically nebulized and aspirated into the primary flame. The combustion products from the primary flame were combined with additional fuel and transported into the analytical flame. The best response and lowest background were obtained when combustion was carefully controlled in the region near the rubidium bead without ignition of the analytical flame. In principle, the system operates as a flameless thermionic detector with liquid introduction and combustion in the primary flame. The optimization of the system was performed in the phosphorus mode with trimethyl phosphate as the model compound. The detector was compatible with organic solvents such as methanol, acetone, ethyl acetate and hexane. A substantial increase in

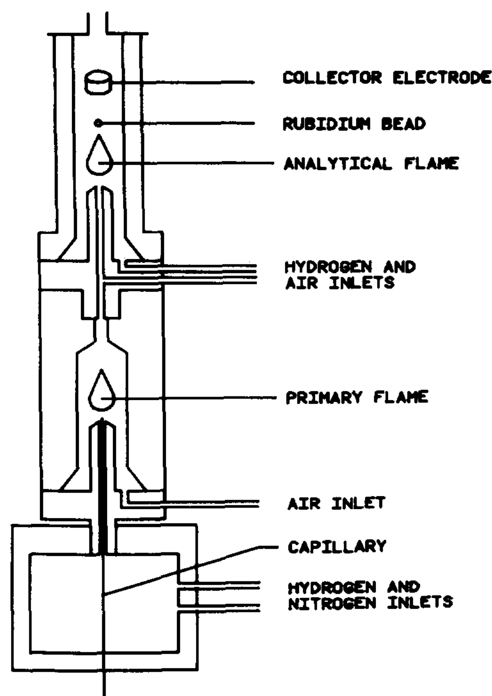


Fig. 9. Schematic diagram of the dual-flame thermionic detector for microcolumn chromatography [44].

background current was observed, however, when using water, acetonitrile or dichloromethane. The minimum detectable amount of phosphorus was found to correspond to 0.5 ng of analyte, and the corresponding average mass flux at the peak maximum was 22 pg/s. The calibration graph was linear over at least three decades of concentration.

With a new version of the thermionic detector [45], the column effluent was orthogonally nebulized and aspirated directly into the primary air–hydrogen diffusion flame. With this approach, the nebulizing efficiency was significantly increased for larger molecules; organophosphorus species having molecular weights >500 could now be detected. As more (organic) effluent was introduced into the flame compared with concentric nebulization, the flame temperature increased, which caused an increase in the background signal. As a result, the detection limits remained similar to those obtained with the former version of the thermionic detector. For the less volatile dimethylthiophosphinic ester of estradiol (MW = 456) the detection limit was ten times higher than for trimethyl phosphate. A linear dynamic range of two decades, instead of the earlier three, was obtained owing to a bipolar orientation at high concentrations.

The LC–TID system has also been optimized for nitrogen sensitivity. In this case, Gluckman and Novotny [46] returned to concentric nebulization directly into the diffusion flame. Detection limits of 14 pg of nitrogen per second at the peak maximum were achieved, with the linearity spanning three orders of magnitude. The applicability

of the system was demonstrated for compounds rather different in molecular weight and tested with microcolumns (0.2 mm I.D.) in addition to open-tubular columns (30–60 μm I.D.). An example of the analysis of underivatized barbiturate standards is shown in Fig. 10.

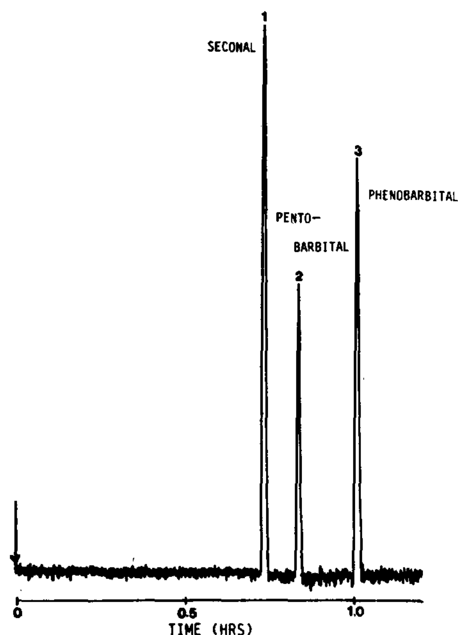


Fig. 10. Chromatogram of three barbiturate standards in their free acid form. Column, 1.8 m × 200 μm I.D., packed with Spherisorb (5 μm) C_8 packing; mobile phase, methanol (1.3 μl/min); injected amount, 20 ng nitrogen per compound [46].

In 1983, Krejci *et al.* [26] demonstrated the use of TID in capillary LC. They stated that when using capillary columns with extremely low flow-rates of 0.001–1 μl/min of organic eluent, the corresponding amount of organic compound introduced is of the same order of magnitude as encountered as a background in GC (column bleeding) when using high temperatures in combination with liquid stationary phases. That is, the detector is operating under average GC conditions, which is very attractive from the point of coupling to LC. However, the interfacing problem still remains. The authors mentioned that the temperature at the end of the capillary column is not too critical for volatile compounds, but should be kept sufficiently high for low-volatile substances. Too high a temperature, however, resulted in clogging of the capillary column due to decomposition of the solutes. The minimum detectable mass flow-rates are 0.1 pg of solute per second for all solutes which are transferred to the detector.

Recently, the use of micro-LC with thermionic detection was extended to the determination of non-volatile polar compounds (see Fig. 11) [47]. An interface, originally developed for the coupling of micro-LC with a flame photometric detector [62], was adapted to TID. Optimization of the detector parameters were studied using the polar non-volatile methylphosphonic acid and its volatile ester dimethyl methylphosphonate as analytes. The system has also been used for the determination of phosphorus-containing pesticide enantiomers [48].

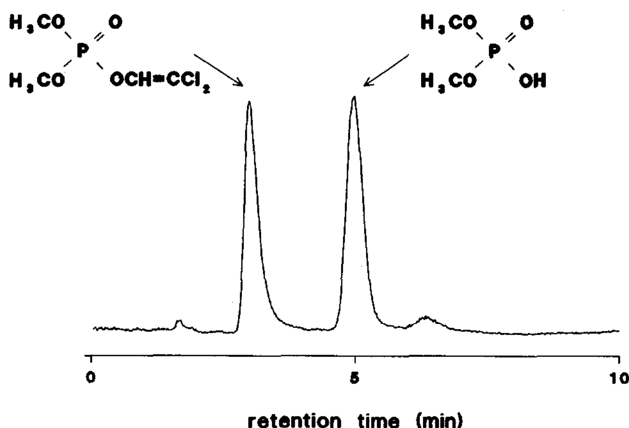


Fig. 11. Micro-LC–TID separation of dichlorvos and its major acidic metabolite dimethylphosphoric acid. Column, PRP-X100, 200 × 0.32 mm I.D.; eluent, 7% ammonium acetate (0.5 *M*) in methanol; flow-rate, 10 μl/min [47].

5.2. *Flameless thermionic detection*

Flameless thermionic detection was coupled on-line to microbore LC by Maris *et al.* [49]. A commercial GC–flameless TID unit was used in combination with 0.7 mm I.D. columns. The set-up allows easy switching from the GC–TID to the LC–TID mode. The evaporation-type interface is a modified version of an earlier developed LC–ECD interface [94], and consists of an aluminium block containing a 150 mm × 0.25 mm I.D. stainless-steel capillary. The temperature of the interface was kept at 300°C. The detection limit was of the order of 5 pg P/s; linear calibration graphs were obtained over at least three orders of magnitude and the selectivity was 10^5 g C/g P.

In a later design [50] (Fig. 12), the vaporized effluent is directed into the base of a GC–TID system via a heated fused-silica capillary. The effluent is swept into the detector using a low flow-rate of nitrogen. With the improved interface, detection limits of 0.2–0.5 pg P/s were obtained for a variety of phosphorus-containing compounds, including several polar pesticides.

The repeatability of the system proved to be good with relative standard deviations (R.S.D.) ($n = 9$) varying from 2% (ethyl-paraoxon and ethylparathion) to 5% (fenitrothion). The performance of this system was further evaluated in a subsequent study [51]. The band broadening of the system proved to be dependent on the volatility of the solutes and on the LC flow-rate. An increased effluent flow-rate decreased the volumetric band broadening considerably for less volatile compounds. This indicates that the type of connection of the capillary between the column and the heated interface is very critical: a thermal gradient existing in the connection capillary should be avoided. This conclusion illustrates the difficulty of vaporizing low-volatility or high-molecular-weight compounds and may well indicate the limitation of evaporation interfaces. In the quoted papers [49–51], trace-level applications to tomato, onion and sediment samples are presented. One such example is shown in Fig. 13.

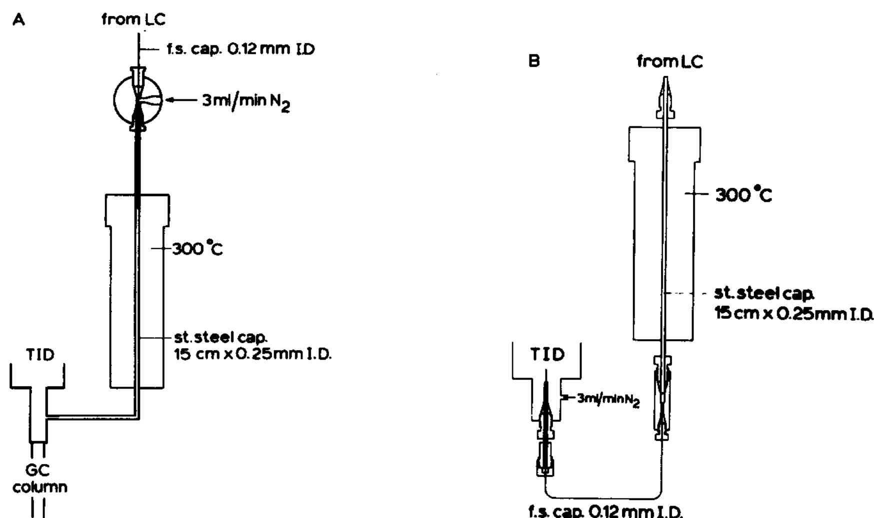


Fig. 12. Schematic diagrams of (A) the original and (B) the modified evaporation interface (ref. 50).

6. FLAME PHOTOMETRIC DETECTION

As early as 1969, Oster [52] reported on the development of a selective detector for LC in the patent literature. The organic LC effluent was evaporated before introduction into a flame photometric detector. In 1975, Freed [53] and, in more detail, Julin *et al.* [54], reported on the on-line combination of ion-exchange chromatography and FPD. The latter group used right-angle pneumatic nebulization and a burner design that allowed the introduction of the mobile phase up to a flow-rate of 5 ml/min. The application of the detector was limited to systems with aqueous mobile phases, because the addition of organic modifiers significantly reduced the detector sensitivity. At 1% methanol, the emission intensity for phosphorus decreased by about 50%. The presence of alkali and alkaline earth metal ions in the mobile phase caused both negative chemical interferences and positive spectral interferences. The system permits the detection of about 0.02 and 0.2 μg/ml of phosphorus and sulphur, respectively. The paper reported interesting applications to non-volatile monophosphate nucleotides and phosphoric acids.

In 1980, Chester [55] also described a flame photometric detector coupled to conventional-size LC. The system utilizes a primary air–hydrogen flame with an inverted configuration, *i.e.*, with air flowing into a hydrogen atmosphere to eliminate solvent interferences, and a secondary flame to measure the molecular HPO emission. In another paper [56] the inverted configuration of the primary flame was compared with the normal configuration. The quenching of the HPO emission by organic compounds is greatly reduced by burning the air–hydrogen flame inside out and the dual-flame configuration has the same advantages as the dual-flame GC detector described by Patterson *et al.* [57,58]. Chester reported an excellent selectivity ratio of about 28 000, a linear dynamic range of 50 000 and a detection limit for trimethyl phosphate of 50 ng of injected compound. The system was used for non-ionic

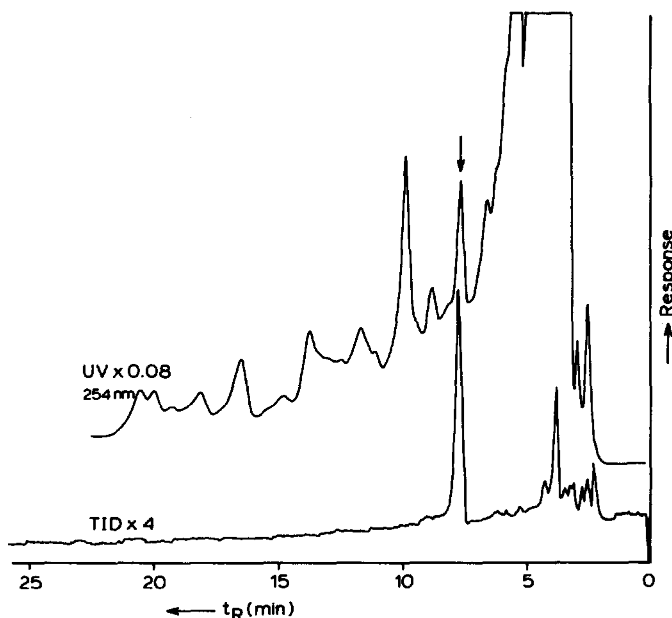


Fig. 13. Reversed phase LC–UV and LC–TID of the extract of an onion spiked with 3.6 ppm of diazinon using LiChrosorb RP-18 with methanol–water (80:20) as eluent; flow-rate, 20 μl/min; UV detection (254 nm), attenuation ×0.08; TID, i_{bc} = 1.6 pA, attenuation ×4 [49].

phosphoric compounds and for ionic species. More recently, Chester *et al.* [59] reported the determination of ortho-, pyro- and tripolyphosphates in detergents; the results agreed closely with values obtained by ion-exchange–autoanalyser systems.

6.1. Miniaturized LC–FPD

The above results indicate that FPD can, to a certain extent, handle reversed-phase LC eluents. One major disadvantage of the commonly used nebulizing interfaces is the low nebulizing efficiency of 15–25%. For a further improvement in the efficiency the introduction of miniaturized LC is recommended: the combination of flame-based detection and micro-LC permits effluent introduction close to or even directly into the flame.

An example of total effluent nebulization into a cool hydrogen–air diffusion flame was first presented by McGuffin and Novotny [60,61]. In principle, the mobile phase introduction was the same as in the micro-LC–TID combination (see Fig. 9). The detector can be used with aqueous mobile phases, while mobile phases containing as much as 50% of methanol, ethanol or acetone (flow-rates of 1–10 μl/min) do not cause a decrease in signal intensity. However, acetonitrile greatly increases the background noise and causes quenching even at low percentages (1–5%). The detector response is linear over two orders of magnitude, with a detection limit of 71 pg/s at the peak maximum for trimethyl phosphate under non-retained (t_0) conditions. Optimum response was obtained with flow-rates below 5 μl/min. Several mixtures of organophosphorus pesticides and dimethylthiophosphinyl derivatives were separated.

In 1987, an interesting alternative was published by Karnicky *et al.* [62] using microbore (1 mm I.D.) and micro (0.32 mm I.D.) LC columns and a virtually unmodified dual-flame photometric detector. Effective nebulization of 2–20 μl/min was obtained using a sophisticated ultrasonic micro-nebulizer. Depending on the mobile phase composition, the flow-rate and radiofrequency power, 10–70% of the LC effluent is nebulized at the excitation point. Droplets less than 10 μm in diameter are swept out of the nebulizing chamber and transported into the detector via the aerosol transport tube and condenser. The authors separated non-volatile phospholipid and sugar phosphate mixtures (Fig. 14). Mobile phases containing buffers caused variations in the nebulizing efficiency; therefore, dual-beam detection was used to improve signal-to-noise ratios and to reduce baseline shifts. With water a detection limit of 50 pg P/s was obtained with a dynamic range of three orders of magnitude. Addition of organic solvents to the mobile phase increased the detection limit to 200–1000 pg P/s, mainly as a result of quenching of the HPO emission.

Folestad and co-workers [63,64] described a chlorine-selective flame-based detector for microbore (1 mm I.D.) LC, in which the total column effluent (20–70 μl/min) is introduced into a heated oven via a spray induced by an electrically heated

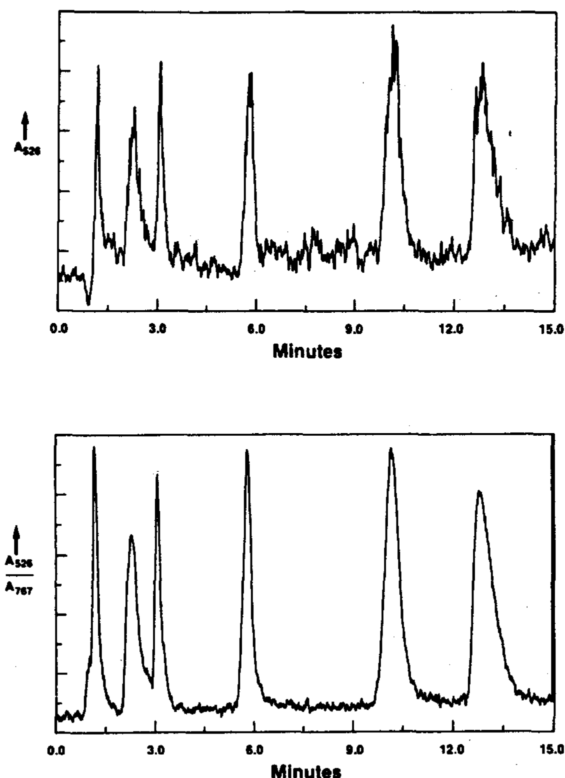


Fig. 14. Illustration of the effect of dual-beam operation. Column, 170 × 0.32 mm I.D. Micropak SP IP-5; mobile phase, 1% *n*-butyl alcohol–0.06% tetrabutylammonium hydroxide–0.12% acetic acid–0.008% perchloric acid; pressure, 304 atm; split flow operation; sample, 0.2 μg each of CMP, 5-AMP, 3-AMP, 2-AMP and cAMP, in order of elution [62].

capillary tip. After pyrolysis in a hydrogen stream, chlorinated compounds are converted into indium(I) chloride in a cool hydrogen diffusion flame and subsequently measured by FPD. The detection limit is 9 pg/s for 1,1,2-trichloroethane in water. In an aqueous mobile phase containing 15% of methanol a linear response was obtained for 5–70 ng of this solute. However, owing to quenching effects the detection limit increased to 115 pg/s. Compounds such as chlorinated uracils, guanine and guanosine could be selectively detected.

Kientz and Verweij [65] coupled a commercially available flame photometric detector to microcolumn (0.32 mm I.D.) LC using an evaporation interface and total effluent introduction. This system was limited to the detection of relatively volatile organophosphorus compounds. In a recent paper, Kientz *et al.* [66] described an improved interface suitable for the detection of non-volatile organophosphorus acids. The total effluent is introduced close to the reaction zone of the hydrogen diffusion flame. For a series of organophosphorus acids, plots of peak area *vs.* amount injected are linear ($r > 0.9998$) in the 0.5–4000 ng range. The repeatability is better than 6% ($n = 148$). The LC–FPD system shows a detection limit of 20 pg P/s when using aqueous solutions containing ammonium formate or acetate, or nitric acid solutions as eluent. With the use of on-line trace enrichment, injection volumes could be increased from 60 nl to 500 μl (Fig. 15), which means that organophosphorus compounds can be detected at concentrations of 5–50 ppb [67].

7. PHOTOIONIZATION DETECTION

Because of the high sensitivity and linearity and also a certain degree of selectivity, photoionization detection (PID) has become an important detection technique in GC. Its potential for GC has been reviewed by Driscoll [68] and Verner [69]. Generally, detection limits are 10–50 times better than those obtained with FID; in addition, PID can detect certain inorganic species and phosphorus- or sulphur-containing compounds. For sulphur-containing compounds, PID is about ten times more sensitive than FPD, with the advantage that linear calibration graphs are obtained.

The ionization of the analytes occurs as a result of the absorption of photon energy, which must exceed the analyte's ionization potential. The photon energy is normally supplied by a suitable UV light source. The ionization potentials for LC solvents typically range from 10.17 eV for hexane, via 10.48 eV for ethanol, 10.85 eV for methanol and 12.22 eV for acetonitrile to 12.59 eV for water. Proper choice of the UV lamp allows the photoionization of many organic compounds, which often have ionization potentials of below 10 eV, with a low background contribution from the LC effluent. Unfortunately, in the liquid state the ionization potential of water is reduced to 6.05 eV [70], that is, with liquid-phase photoionization the use of reversed-phase LC is ruled out and application is limited to normal-phase LC. The use of gas-phase PID after evaporation, *i.e.*, coupling LC to a gas-phase PID system, is therefore interesting.

Preliminary work on LC–PID was carried out by Schmermund and Locke [71]. In their set-up, the normal-phase effluent (1 ml/min) was completely vaporized in a modified Hamilton injection port. Solvents such as *n*-pentane, diethyl ether, methanol and their mixtures could be used. No signal was obtained with these solvents when a lithium fluoride (11.9 eV) window was used on the discharge tube. The

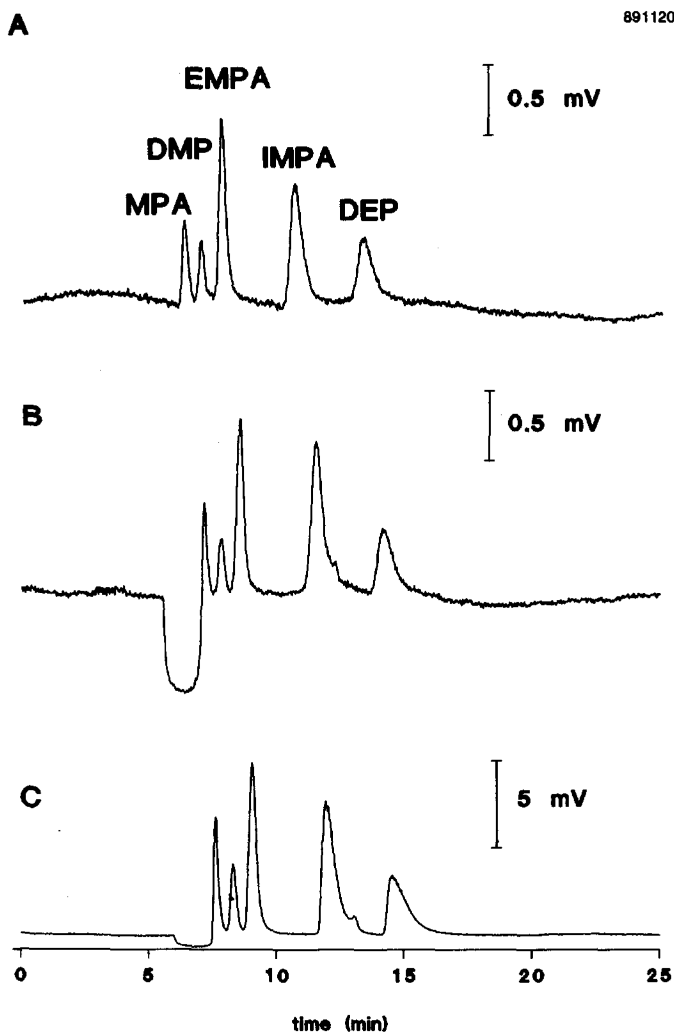


Fig. 15. Trace enrichment of organophosphorus acids with (A) direct injection of 60 nl of test mixture (0.5–3 mg/ml), (B) and (C) 60 and 500 μl, respectively, injection of the 1000-fold diluted test mixture via a precolumn. Eluent, 0.5 *M* ammonium acetate (pH 5); flow-rate, 6 μl/min; column, 700 × 0.32 mm I.D. fused-silica capillary packed with 10-μm PRP-1. Precolumn (4 × 1 mm I.D.) packed with 10-μm MA-100 polymeric anion exchanger. MPA, methylphosphonic acid; DMP, dimethylphosphoric acid; EMPA, ethylmethylphosphonic acid; IMPA, isopropylmethylphosphonic acid; DEP, diethylphosphoric acid [67].

relatively low maximum temperature of 80°C limited the use of solvents with higher boiling points. From the mass flow-rate of methylaniline producing a peak twice the noise level, a detection limit of 10 pg/s was calculated. The linear dynamic range was 10^4. More recently, Locke *et al.* [72] compared results obtained with liquid-phase and gas-phase PID. With regard to gas-phase PID, they concluded that the great advantage is the ability to accept reversed-phase effluents; the real applications will probably be found in miniaturized LC with flow-rates below 10 μl/min.

In 1984, Driscoll *et al.* [73] evaluated the applicability of LC–PID for the determination of specific classes of analytes, using reversed-phase eluents. A schematic diagram of their system is shown in Fig. 16. The separations were carried out on conventional C_8- or C_{18}-bonded silica columns, with acetonitrile–water or methanol–water mixtures at flow-rates of 0.5–2.5 ml/min as mobile phase. The liquid effluent was led into a heated interface oven providing complete evaporation of the mobile phase; after (variable) splitting of the vaporized effluent and addition of helium carrier gas, the gas stream was transported to the detector. The heated interface allows the introduction of both aqueous and organic mobile phases. The system was tested with analytes such as aromatic and aliphatic amines and substituted hydrocarbons. The detection limits varied from 3 to 700 ng, and were determined by the nature of the analytes, the carrier gas and the applied lamp energy. The lowest detection limits were observed for analytes having electronegative groups, and when working at relatively low flow-rates of 0.5 ml/min, with helium as carrier gas. Compounds with ionization potentials in the range 7–8 and 8.5–9.5 eV, showed a response improvement of one order of magnitude when 9.5-eV (instead of 10.2-eV) and 10.2-eV (instead of 9.5-eV) lamps were used, respectively.

Yang *et al.* [11] coupled PID to a transport system based on thermospray vaporization, as discussed above in the section on interfacing. Their system was used for the detection of amino acids and peptides, with water as mobile phase, in both a flow-injection and an LC separation system. The detection limit for phenylalanine was 2 ng and the linear dynamic range was $> 10^4$.

7.1. Capillary chromatography

Recently, De Wit and Jorgenson [74] reported on the coupling of vapour-phase PID to open-tubular LC. The three major processes, vaporization, ionization and ion collection, could be studied separately owing to the special detector design (Fig. 17). The vaporization of the LC effluent is accomplished by a fine heating wire placed over the column end. To prevent plugging caused by extensive heating of the column end, the wire is pulse-heated ohmically so that the effluent vaporizes as it leaves the column. Cooling was facilitated by an additional helium carrier gas flow. A 10.02-eV krypton discharge lamp was used as the light source. Parameters such as the electrical potential, helium flow-rate and detector temperature were optimized using toluene as a test solute [ionization potential (*IP*) = 8.82 eV] and acetonitrile (*IP* = 12.20 eV) as mobile

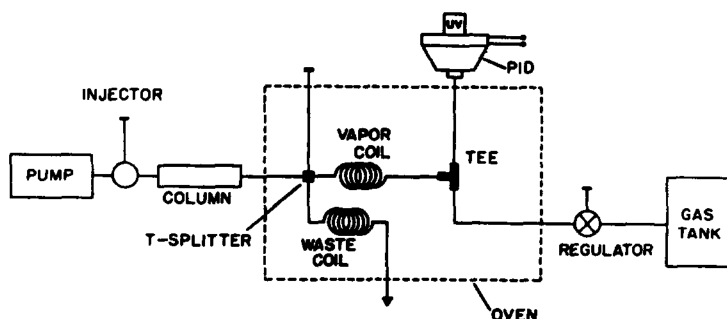


Fig. 16. Schematic diagram of the LC–PID system [73].

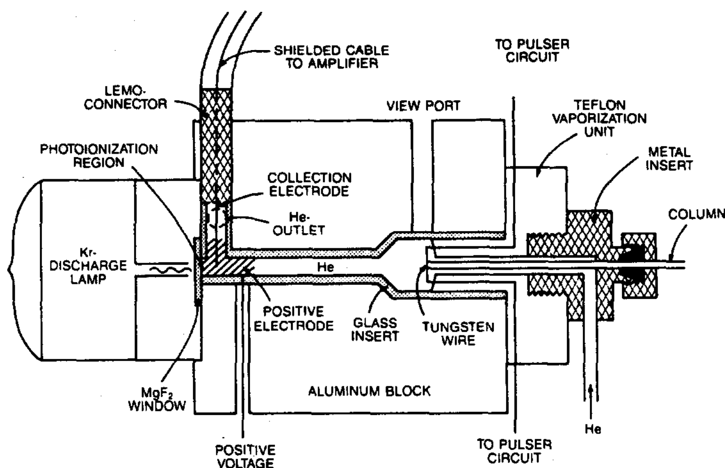


Fig. 17. Schematic diagram of the photoionization detector [74].

phase so that toluene was ionized without ionization of the acetonitrile. An example of the analysis of a mixture of pesticides is shown in Fig. 18. The response of four analytes *versus* their concentration showed good linearity (slope of log–log response >0.9986); the detection limit for toluene was 5 μM.

8. ELECTRON-CAPTURE DETECTION

As early as 1968, Maggs [75] published the first results on LC–ECD coupling. The author used the Pye Unicam moving-wire system which had recently become commercially available, and replaced the flame ionization detector by a Pye Unicam electron-capture detector. He obtained a high detection limit of 10 ng/ml after the separation of lindane and dieldrin on alumina using hexane–ethanol (95:5) as eluent. Since these early attempts, it has been convincingly shown that the low response of

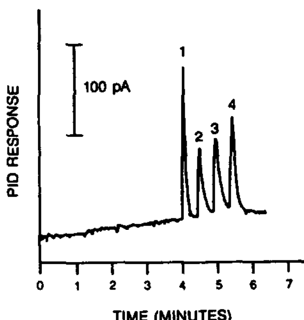


Fig. 18. Chromatogram of a mixture of pesticides. The separation was carried out on a 1 m × 10 μm I.D. fused-silica column coated with OV-17-V. The mobile phase was acetonitrile–water (50:50) at a flow-rate of *ca.* 100 nl/min. The pulsed heating wire was used, and the detector block was operated at 200°C. The helium flow-rate was 20 ml min. Peaks: 1 = metribuzin; 2 = fenthion; 3 = ametryn; 4 = prometryn; all at a concentration of 1 mg/ml [74].

ECD towards various types of LC mobile phases permits a more direct on-line set-up. This will be discussed in the next section.

8.1. Direct introduction LC–ECD

In 1971, Nota and Palombari [76] presented an on-line LC–ECD system using a nebulizer interface. The effluent is nebulized continuously and part (*ca.* 10 μl/min) is admitted into the detector. The following effluents could be used without serious problems: lower alcohols, benzene, hexane, cyclohexane, pyridine, diethyl ether and acetone. The significant additional band broadening due to the nebulizer was probably the reason why no follow-up of this work has been published. However, the basic design is interesting, as it is the most direct type of LC–ECD interfacing reported so far.

In most of the work published since 1974 vaporizing interfaces were used, based on the work of Willmott and Dolphin [77]. The total LC effluent is vaporized in a stainless-steel tube mounted in an oven maintained at 300–350°C; from this, the vapour is forced by an additional nitrogen purge through the electron-capture detector and, finally, into a metal condenser which acts as a trap for radioactive material. This approach was applicable with normal-phase LC using conventional columns. The system has been commercially available for several years through Philips (Eindhoven, Netherlands). A successful application was the development of an automated instrument for the determination of pesticides in milk [78]. The detection limits of the pesticides in milk fat were below 0.1 mg/kg. Another application was presented by Demeter and Heyndrickx [79] for the determination of the relatively polar pesticide endosulfan in serum and urine samples (Fig. 19). A detection limit of 200 pg of α-endosulfan and linearity within a range of 500 agreed within the manufacturer's specifications.

As regards the mobile phase, which, in the initial stages, almost invariably was isooctane or hexane and, more recently, also toluene, there was of course a strong need for dry solvents completely free from electron-capturing impurities. The initial problems in this area were solved by refluxing the solvents for 1 h with a 45% dispersion of finely divided sodium in solid paraffin, which resulted in a much reduced background noise [80]. It was also shown that the addition to the mobile phase of 10–15% of a polar modifier such as dioxane or a few percent of a lower alcohol can be tolerated with only a marginal increase in the background [81]. Several interesting applications were published on LC–ECD in the normal-phase mode. Krull and co-workers [82,83] interfaced a conventional liquid chromatograph to an electron-capture detector using the GC system as vaporization unit. They used their system for the trace-level determination of explosives such as 2,4,6-trinitrotoluene, 2,4-dinitrotoluene, pentaerythritol tetranitrate and 1,3,5-trinitro-1,3,5-triazacyclohexane in post-blast residues. With a splitting ratio of 10:1, the detection limits (signal-to-noise ratio = 3) are 0.1–1 ng with a linear response over four orders of magnitude.

Further optimization of LC–ECD interfacing was studied by De Kok *et al.* [84]. They designed a new (shorter and smaller bore) coiled evaporation-type interface which fits snugly in the grooves of a cylindrical metal block; this results in improved heat transfer. The advantages of the new interface design compared with the commercial one were an improved performance, allowing the detection of higher boiling halogenated aromatics, and a reduction in additional band broadening.

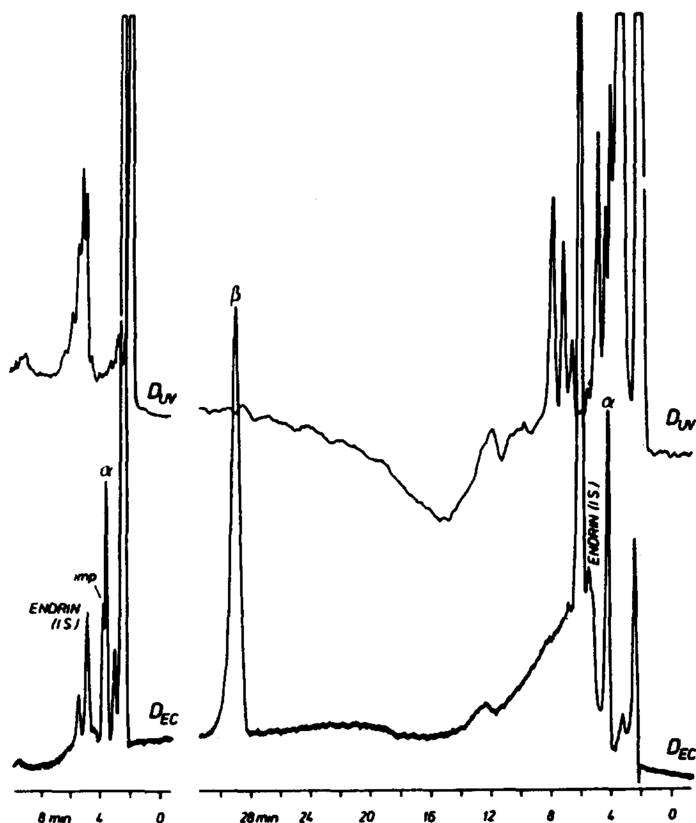


Fig. 19. Liquid chromatogram of a spiked liver extract containing 50 ng of α- and 200 ng of β-endosulfan. Right: no clean-up by liquid–liquid partitioning. Left: preliminary clean-up by liquid–liquid partitioning [79].

Detection limits for diverse types of halogenated compounds were in the 5–100 pg range and the system proved to be linear over three orders of magnitude. In further work, the authors extended the application range of LC–ECD to more polar compounds such as substituted anilines, chlorophenols and hydroxylated polychlorobiphenyls, and also to phenylurea herbicides, by applying derivatization with heptafluorobutyric anhydride (HFBA) [85]. The detection limits of the phenylurea herbicides in surface water were far below the 1 ppb level [86]. Further applications are the determination of chloroxuron as its HFB derivative in strawberries, with a detection limit of 20 ppb [87], and the determination of pentachlorophenol in wood samples [88] and, down to 5–10 ppb, in liver samples [89].

An interesting development to make conventional reversed-phase LC compatible with ECD was published by Maris *et al.* [90]. They designed a post-column extraction module in order to be able to use aqueous LC eluents containing non-volatile ion-pairing agents, with hexane, toluene and their mixtures (generally 1:1) as extraction solvents. The general set-up is shown in Fig. 20. Using methanol–water mixtures at an (LC) flow-rate of 1 ml/min, a detection limit of 500 pg was found for

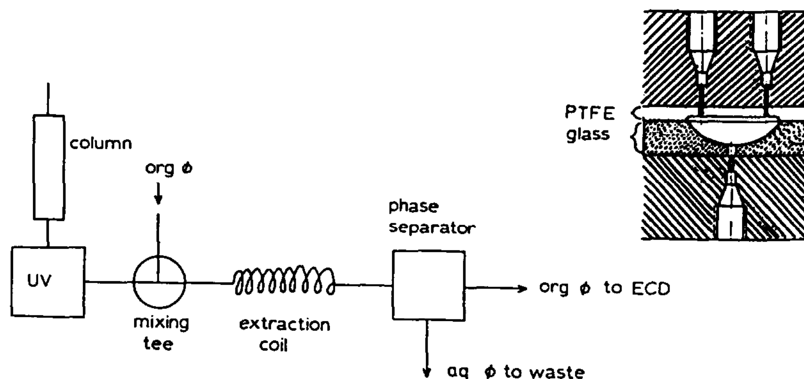


Fig. 20. Schematic design of the reversed-phase LC–ECD system, coupled via a post-column extraction module. The detailed construction of the phase separator is shown as an inset [90].

pentachlorophenol, with an acceptable total post-column band broadening compared with the contribution of the evaporation interface. As a follow-up, a paper was presented on the separation of nitroaromatics and chlorinated pesticides [91]. Combination of this set-up with on-line trace enrichment has allowed the determination of pentachlorophenol in urine samples at the 4 ppb level (see Fig. 21) [90].

Improved detection limits in LC–ECD were reported by Krull and Bushee [82] when applying very low flow-rates. In addition, the early results of Nota and Palombari [76] indicated that small amounts of solvents typically used in reversed-phase chromatography can be tolerated in LC–ECD. In other words, reduction of the flow-rate by applying miniaturized LC is a promising approach to extend the application range of LC–ECD.

8.2. Miniaturized LC–ECD

In 1983, Brazhnikov *et al.* [92] used ECD to test the performance of microbore (1 mm I.D.) columns in the normal-phase LC mode. They coupled the detector directly to the LC column and compared their results on extra-column band broadening with results obtained with a UV detector having a 1-μl cell volume. They found an acceptable extra-column band broadening of 1.4 μl at an eluent flow-rate of 30 μl/min. The loss in efficiency at flow-rates of 30–50 μl/min did not exceed 5%.

In 1984, Brinkman *et al.* [93] showed the applicability of miniaturized LC–ECD (0.7–1 mm I.D. columns; flow-rates of *ca.* 50 μl/min) for both normal- and reversed-phase LC. This was an important step forward in on-line LC–ECD coupling, because in this instance reversed-phase LC was combined with ECD using total effluent introduction. For reversed-phase LC a Hypersil ODS column (1 mm I.D.) was used with methanol–water (85:15) at a flow-rate of 50 μl/min as the mobile phase. The mobile phase was evaporated at 300°C using a miniaturized interface, *viz.*, a 300 mm × 40 μm I.D. nickel capillary. A linear calibration graph was obtained for 2,6,2′,6′-tetrachlorobiphenyl over 2–3 orders of magnitude with a detection limit of 100 pg. Subsequently [94], the same group studied the mobile phase composition. Methanol and dioxane are clearly preferable to acetonitrile as organic modifiers; considerable noise reduction can be obtained by thoroughly degassing the eluent.

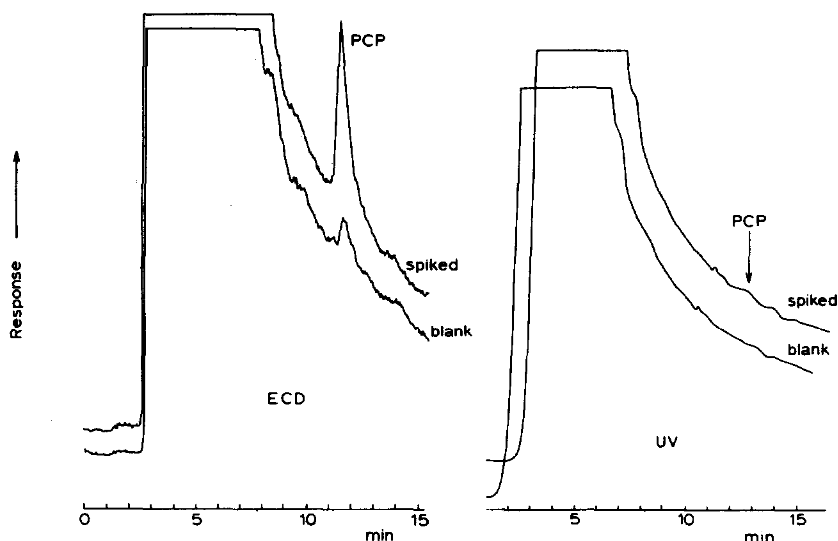


Fig. 21. Reversed-phase LC–extraction module–ECD and reversed-phase LC–UV detection for a urine sample spiked with 10 ppb PCP and a blank urine sample, both obtained after on-line preconcentration of 2.3 ml (onto the column); 25% of the extraction solvent was directed to the electron-capture detector [90].

Surprisingly, the LC–ECD system can even be used with pure water (at 20 μl/min) as eluent. Several successful separations have been reported; an example is given in Fig. 22. It was also shown that the addition of acids such as acetic or formic acid or of triethylamine to the mobile phase can be tolerated. However, under acidic conditions peak distortion was occasionally observed, probably owing to the use of nickel tubing in the interface. In a later stage [95], the nickel tubing was replaced with a fused-silica capillary, which gave an acceptable extra band broadening (including the detector) of 1 μl^2 at an effluent flow-rate of 25 μl/min. The system was applied in the normal-phase mode and was the first to be used for gradient elution with hexane–toluene mixtures. The baseline stability is high and the detection limits of suitable electron-capturing compounds are of the order of 1 pg; calibration graphs are linear over three orders of magnitude. The LC–ECD applications published in the literature are summarized in Table 2.

9. GAS-PHASE CHEMILUMINESCENCE DETECTION

When chemical reactions result in the formation of compounds that are electronically or vibrationally excited, the resulting photon emission is called chemiluminescence. In the past decade, GC detectors based on this principle have been developed and their high selectivity has repeatedly been demonstrated [1]. For the determination of nitrosamines and nitrosamides, a GC detector, the thermal energy analyser (TEA), has been developed by Fine and co-workers [97–99] (see Fig. 23). This instrument is commercially available from Thermo Electron (Waltham, MA, USA). Subsequently, the use of TEA in combination with LC was demonstrated [100,101]. The LC effluent which may contain both volatile and non-volatile N-nitroso

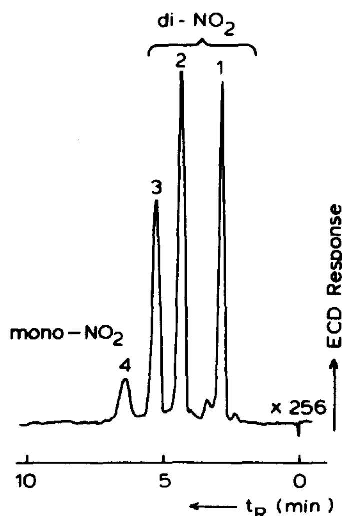


Fig. 22. Reversed-phase LC–ECD for injection of 6 ng of nitroaromatics using LiChrosorb RP-18 with methanol–water (80:20) as eluent. Flow-rate, 35 μl/min; attenuation, ×256. Solutes: 1 = 2,4-dinitrophenol; 2 = 2,4-dinitroaniline; 3 = 1,3-dinitrobenzene; 4 = 4-nitrotoluene [90].

TABLE 2

APPLICATIONS OF LC–ECD

Class of compounds	Matrix	Ref.
Pesticides	Milk	78
	Serum, urine	79, 91
Explosives	Post-blast residue	82, 83
Nitroaromatics	Urine	91
Phenylurea herbicides	Surface water	84
	Strawberries	87
Pentachlorophenol	Wood, liver	88, 89
Chlorophenols	River water, urine	96

compounds, is led into a pyrolysis oven together with a flow of argon or nitrogen carrier gas. In the oven catalysed pyrolysis of N-nitroso compounds takes place and nitric oxide is formed according to

$$R^1R^2N\text{–}NO \rightarrow NO^{\bullet} + R^1R^2N^{\bullet} \quad (1)$$

The heated gas and vapours subsequently pass two cold traps; the first trap serves to liquefy the effluent and the second to remove all remaining solvent vapours and decomposition products. Owing to its high vapour pressure, even at −150°C, nitric oxide passes through the second cold trap, whereas most potentially interfering organic compounds are retained. In the reaction chamber, chemiluminescence is induced according to the following reactions:

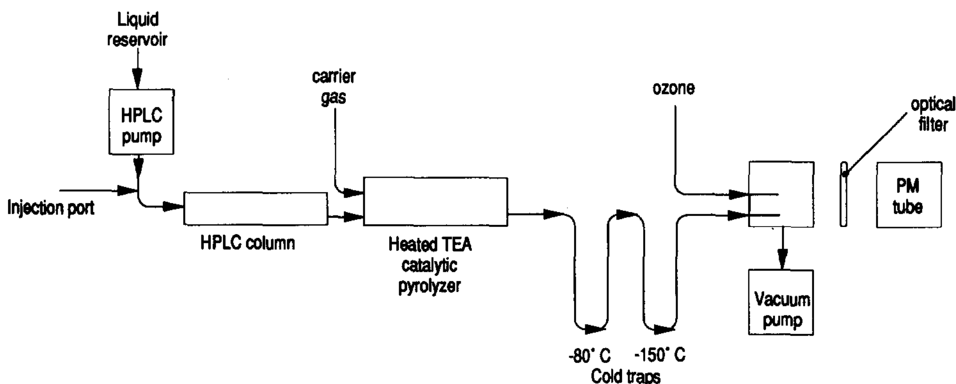


Fig. 23. Schematic diagram of the LC–TEA interface [101].

$$NO^{\bullet} + O_3 \rightarrow NO_2^* + O_2 \quad (2)$$

$$NO_2^* \rightarrow NO_2 + h\nu \quad (3)$$

The intensity of the emitted light is proportional to the number of nitrosyl radicals present and is measured by an infrared-sensitive photomultiplier. If the pyrolysis oven is kept at 500°C, the system is highly selective for N-nitroso compounds.

In GC, when applying temperatures of up to 800°C, nitro compounds decompose and form nitric oxide; this extends the use of the TEA to aromatic nitro compounds and explosives. Unfortunately, in the LC mode the operating temperature of the pyrolysis oven has an upper limit of 550°C because of baseline noise. Therefore, LC–TEA is always operated in the nitroso mode. The dead volume of both solvent traps (see Fig. 20) is less than 10 μl of mobile phase. This is accomplished by reducing the pressure inside the traps from 760 mmHg (100 kPa) to less than 4 mmHg (0.5 kPa), thus reducing the 300-ml trap volume to less than 1.7 ml. The linearity of the system is over four orders of magnitude, and the sensitivity is *ca.* 1 ng/ml for N-nitroso compounds with the use of 40-μl injections.

The characteristics of LC–TEA were described by Baker and Ma [102]. They found that the response of the TEA detector is highly dependent on the operating temperature of the furnace and on the flow applied to purge it. The response also depends on the volatility of the nitroso compounds, which results in different operating conditions for low- and high-volatile nitroso compounds. Under optimum conditions a minimum concentration sensitivity of 3–5 μg/ml was found for these compounds, which is *ca.* 100 times poorer than levels obtained by others [100,101,112, 127]. One limitation of the LC–TEA system is that the considerable amounts of LC effluent require a constant cleaning of the cold traps, which implies repeated interruption of the analyses. In 1981, Widmar and Grolimund [103] solved this problem by using a secondary vacuum system to empty the cold traps. LC–TEA cannot be operated with aqueous effluents or inorganic buffer solutions.

As was stated above, nitroaromatics are not readily detected at a pyrolysis oven temperature of 550°C. This is due to the significantly higher bond energy (292 kJ/mol) of the C–NO_2 bond of nitroaromatics compared with the N–N bond energy (159

kJ/mol) of nitrosamines and the O–N bond energy (175 kJ/mol) of nitrate esters. In order to improve the detection of nitrotoluenes, in 1987 Selavka *et al.* [104] introduced photolytically assisted thermal energy analysis (LC–PAT). They used UV irradiation to induce C–NO_2 bond cleavage, releasing NO_2 which is suitable for TEA detection. The release of NO_2 was confirmed using batch irradiation followed by LC–TEA, which resulted in the identification of mono-, di- and trinitrotoluenes. In order to reduce the band broadening, a knitted open-tubular photochemical reaction detector design was used, with a 0.6 mm I.D. knitted PTFE tube having a volume of 6 ml. The use of LC–PAT improved the TEA detectability of tri- and dinitrotoluene by a factor of 30 and 16, respectively. The former compound now had a detection limit of 0.5 ng; its response was linear over three orders of magnitude (0.1–100 ppm). Mononitrotoluene could be detected at the sub-nanogram level in the LC–PAT mode, whereas 60 ng of this compound could not be detected when the UV lamp was turned off.

The applications of LC–TEA reported in the literature are listed in Table 3. Krull *et al.* [105] have reviewed the determination of N-nitroso contaminants in biological samples.

In 1988, Robbat *et al.* [133] coupled a gas-phase chemiluminescence detector, which was originally developed for the GC of polycyclic nitroaromatics [134], to LC. The operating principle is based on the well known nitric oxide–ozone reaction. In GC the pyrolysis chamber is kept at 1000°C in order to form nitrosyl radicals. In contrast to results on LC–TEA mentioned above, the pyrolysis oven temperature is kept at a relatively high value of 900°C without baseline instability. In addition, the use of aqueous eluents is allowed. The system was used for the reversed-phase LC of nitroaromatics utilizing a 2.1 mm I.D. column and relatively low flow-rates of 0.2–0.5 ml/min. The detection limit increased from 30 ng of injected 1-nitronaphthalene in

TABLE 3

APPLICATIONS OF LC–TEA ANALYSIS

Class of compounds	Matrix	Ref.
N-Nitroso	Water	106
	Food	107, 108
	Blood	109
	Animal	110
Nitrosamines	Food	125
	Cutting fluid	114, 137
	Cosmetics	112, 126, 127 128, 129, 116
	Rubber	132, 124
Nitrate esters	Explosives	126, 122, 121, 131
Nitroglycerine	Plasma	111, 118, 122, 132
Isosorbide dinitrate	Plasma	113, 132
Pentaerythritol	Plasma	132
Methylated N-nitroso acids and dipeptides		130
Nitrotoluenes	Explosives	104

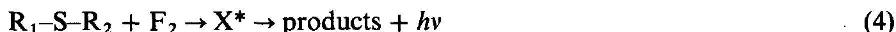
pure acetonitrile to 250 ng of injected analyte in acetonitrile–water (50:50). Linearity was observed between 70 and 1000 ng for ten nitroaromatics using a reversed-phase linear gradient.

9.1. Miniaturized LC–chemiluminescence detection

In 1982, Massey *et al.* [135] used microbore (1 mm I.D.) LC–TEA to permit work with aqueous eluents and ion-pair reagents, in order to be able to determine polar and ionic nitrosamines. The LC effluent, methanol–water (70:30) containing 0.1 *M* ammonium heptanesulphonate at a flow-rate of 20 μl/min, was mixed with acetone (2 ml/min) and introduced into the pyrolyser oven operated at 650°C. Fig. 24 shows the chromatogram recorded for the ionic nitrosamine N-nitroso-N^1,N^1-dimethylpiperazinium iodide.

In 1985, Rühl and Reusch [123] used microbore LC–TEA to determine N-nitrosamines by means of normal-phase LC; the pyrolyser oven was operated at 500°C. Flow-rates of 60–80 μl/min allowed the system to be operated continuously. They compared their results on the analysis of nitrosatable compounds in rubber nipples with those of GC–TEA, and found good agreement.

For the detection of organosulphur compounds, a gas-phase chemiluminescence detector has been developed by Mishalanie and Birks [136]. Detection is based on the chemiluminescence reaction that occurs when certain sulphur-containing compounds react with molecular fluorine:



$$R_1\text{–S–}R_2 + F_2 \rightarrow X^* \rightarrow \text{products} + h\nu \quad (4)$$

where X* is an electronically or vibrationally excited species which, based on spectroscopic studies, can be HF, CH_2S, HCF or FCS. The emission is viewed through

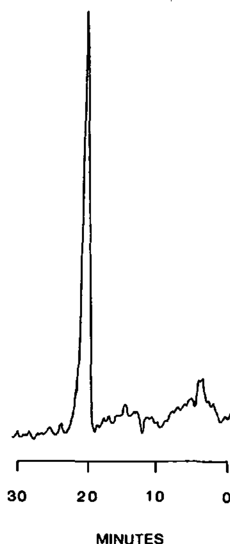


Fig. 24. Reversed-phase ion-pair LC–TEA of N-nitroso-N^1,N^1-dimethylpiperazinium iodide (105 ng). TEA attenuation, ×16 [135].

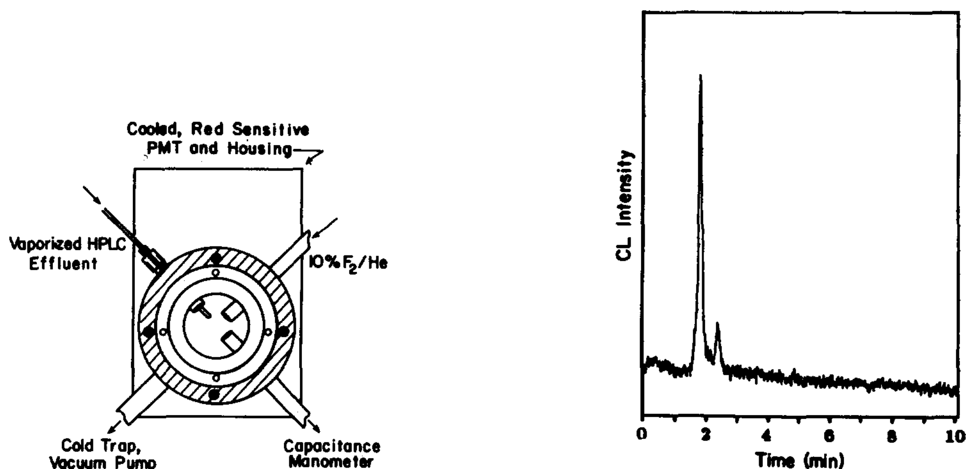


Fig. 25. Front view of the detector cell [136].

Fig. 26. Chromatogram of a filtered beer sample. The peak at 1.8 min corresponds to about 1 ng of dimethyl sulphide. Chromatographic conditions: acetonitrile–water (70:30) at a flow-rate of 80 μl/min; sample, 1 μl [136].

quartz windows and measured by a cooled red-sensitive photomultiplier using a filter accessible to wavelengths between 659 and 800 nm. The front view of the detector cell is shown in Fig. 25. The microbore LC column is interfaced to the detector cell by means of a 100 × 0.254 mm I.D. stainless-steel capillary which is wrapped with heating take and maintained at 300°C to vaporize the column effluent. The system was used to detect a number of sulphides, disulphides, thiols, the sulphur-containing pesticides malathion and parathion and dimethyl selenide and dimethyl diselenide. For most organosulphur compounds the detector response is linear over three orders of magnitude and detection limits are from 50 pg to 3 ng of analyte. Fig. 26 shows the determination of dimethyl sulphide in a filtered beer sample.

10. CONCLUSIONS AND FUTURE PROSPECTS

The present literature research revealed that, especially in the past decade, much attention has been devoted to the on-line coupling of column LC and GC-type detectors. Use of GC-type detectors will often lead to increased sensitivity and, even more important, increased selectivity of the LC procedure. As is to be expected in every situation in which two more or less incompatible systems or system parts have to be coupled in an on-line mode, much effort has gone into the design and construction of proper types of interfaces which, obviously, cannot be the same for every type of GC detector studied. In many instances, successful solutions to the various problems have been found, miniaturization of the LC part of the system frequently having been introduced to promote the viability of the on-line coupling approach. The real success of the column LC–GC-type detector coupling is probably read best from the many real applications that have been published and from the notable success of LC–ECD coupling in both normal- and reversed-phase LC.

A series of more detailed comments on the present state and future prospects of the various column LC–GC-type detector systems discussed so far is given below.

10.1. Interfacing

Transport systems and the (often fairly simple to construct) vaporizing devices share the disadvantage of possible loss of analytes, *viz.*, of volatile and non-volatile compounds, respectively. Although further development of these devices should not be neglected, total LC effluent introduction from miniaturized LC systems or by using spraying devices, induced by gas flow or thermal effects, is probably a more interesting alternative, because the complete transport of all analytes into the detection zone is now being achieved. Admittedly, with miniaturized LC an important practical problem is the low sensitivity in terms of concentration units, which is a direct result of the small injection volume. Except for those instances where sample volumes are limited, the development of suitable on-line trace enrichment techniques should therefore be given priority: most of today's real LC applications require a sensitivity at the ng/ml level.

An interface-related problem that often is not recognized is the solubility of the silica column packing materials in aqueous eluents with pH values higher than 5–6 [67]. Even before a distinct decrease in separation efficiency and/or baseline instability are observed, clogging of the interface can occur. The introduction of pressure-resistant and efficient polymer-based packing materials may well provide a solution here.

10.2. LC–FID

For this combination, transport systems have been improved significantly over the years. Miniaturized LC, in combination with transport systems, permits total effluent introduction and, thus, better sensitivity. On-line interfacing of capillary LC to FID has shown that the detector can handle a total solvent flow of about 1 μl/min. When water-containing effluents are used, miniaturized on-line LC–FID may be a promising technique for the determination of ionic and polar organic species. Organic effluents, unfortunately, induce an increased base current and reduced sensitivity, which makes them less desirable. In other words, for the use of universal solute detection using organic LC eluents, the transport flame ionization detector is still the best solution.

10.3. LC–TID/NPD

Both dual-flame TID and flameless TID have been discussed in the literature. On-line coupling of both detectors to miniaturized LC systems has resulted in the detection of trace amounts of both phosphorus- and nitrogen-containing compounds. A reliable comparison of the two systems is difficult, because inherently different interface principles, such as direct liquid introduction and evaporation, have been used. The main limitations are that neither system can be used with LC effluents containing inorganic buffers or salts and that most non-volatile analytes cannot, as yet, be handled.

10.4. LC–FPD

When coupling FPD on-line to a conventional LC system, the sensitivity is low; in addition, the use of organic modifiers dramatically reduces the sensitivity. The influence of the flame configuration on the quenching effect, which, *e.g.*, reduced quenching when burning the flame "inside out" [56], should be further investigated. With microbore LC (1–0.7 mm I.D.) and micro-LC (0.5–0.1 mm I.D.), total LC

effluent introduction is possible. The sensitivity distinctly increases and even non-volatile organophosphorus compounds can now be analysed. The use of micro-LC is most promising because the effluent flow of, typically, less than 5 μl/min also permits the use of organic modifiers because of the reduced total amount of carbon introduced per second.

10.5. LC–PID

Only a few papers have been published on on-line LC–PID. However, the further development of this technique, especially when using miniaturized LC, may well yield a promising alternative to LC–FID. By using a UV source with a photon energy output below the ionization potentials of water and acetonitrile, which are relatively high in the gas phase, it should be possible to determine a substantial number of organic compounds with a minimum background contribution.

10.6. LC–ECD

On-line LC–ECD is the combination that has been discussed most frequently and a number of interesting applications have been published; these mainly deal with normal-phase LC. However, distinct successes have also been reported in the area of reversed-phase LC. For example, when using microbore LC columns, total effluent introduction was permitted even with mainly aqueous LC eluents. Further studies in this direction certainly are of great interest. Such studies should include further work on interface design. At present, the interface principle in LC–ECD generally is based on vaporizing the total effluent; this limits the possibility of handling relatively non-volatile and/or polar compounds.

10.7. LC–chemiluminescence detection

In the past, LC–TEA has clearly proved its importance in the determination of N-nitroso compounds which are potential carcinogens. Recent developments, such as utilizing miniaturized LC and working with photolytically assisted TEA, are extending the application range to more polar and ionic nitrosamines and nitroaromatics and the use of aqueous buffer solutions.

Miniaturized LC combined with gas-phase chemiluminescence, with its excellent sensitivity and selectivity, may well turn out to become an important tool in environmental analysis.

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