Low Pressure - Gas Chromatography: Recent Trends and Developments

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Abstract

Low pressure - gas chromatography (LP-GC) has been applied during the last few years for the fast analysis of various pollutants in different environmental and food matrices. A typical LP-GC setup involves the use of a short microbore column (typically 0.5 - 1 m x 0.10 mm internal diameter) at the injector side connected with a zero dead-volume connector to a short megabore column (typical 10 m x 0.53 mm) to be used with higher gas velocities. This setup maintains atmospheric injection conditions, while the analytical column is operated under low pressure conditions which are compatible with mass spectrometer analysers. Although the use of LP-GC results in a loss of separation efficiency, it offers a 3-5 fold reduction in analysis time for organic compounds and thus an increased sample throughput and an enhancement of the signal to noise ratio leading to improved detection limits. Considering the significance and the potential interest for this topic, the present review briefly describes the concept of LP-GC. Furthermore, the recent developments and applications of LP-GC, with a focus on the use of various column systems and analyzers, are also explored. Finally, the prospects and limitations of LP-GC are also critically evaluated.

Keywords: fast gas chromatography, low pressure – gas chromatography, hyphenated techniques, review

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1. Introduction

Speeding-up the analysis has always been a need in gas chromatography (GC), because shorter analysis times provide a higher throughput and reduced costs. In GC, the application of vacuum column-outlet is an attractive way to speed-up the analysis. Cramers et al. [1] summarised the existing methods to minimize the analysis time in GC and, recently, Mastovska and Lehotay [2] reviewed the main approaches to fast GC coupled to mass spectrometry (MS). These approaches includes i) the use of a short microbore (0.1 mm internal diameter-I.D.) capillary GC column; ii) fast temperature programming; iii) low-pressure GC–MS using a megabore (0.53 mm I.D.) column; iv) supersonic molecular beam for MS at high carrier gas flow; and v) pressure-tunable GC x GC [2].

Until now, limited interest has been paid to evaluate the possibilities of operating columns at reduced pressure [3], so-called vacuum outlet capillary GC, vacuum GC or low pressure (LP) – GC (Figure 1). Recently, Donato et al. [4] provided an overview of fast GC techniques for the analysis of food constituents and contaminants, but only few applications of LP-GC were described despite several attractive features of this technique. As demonstrated by Cramers et al. [3], the use of a short megabore column may lead to a considerable gain in speed [5-7], while Amirav et al. [5] concluded that a short megabore column, such as used in LP-GC, provided similar or even superior analytical performances for fast GC than a short microbore capillary column. Moreover, in contrast to other fast GC methods, the LP-GC setup had significantly increased sample capacity.

The present review provides a basic introduction to LP-GC, together with a summary of parameters that need to be optimized for successful LP-GC. This review also aims to summarise recent developments of LP-GC for various industrial, food and environmental applications.

2. The concept of low pressure-gas chromatography (LP-GC)

The principles and theory together with speed-optimization strategies in gas-chromatography have been already clearly defined by other authors [1, 3, 8-10] and, therefore, a theoretical detailed description of the LP-GC technique will not make the subject of the present review. Instead, a brief discussion of the principal parameters which influence the use of LP-GC is given below. Throughout the review, the following column terminology was used: megabore column for 0.53 mm I.D.; widebore column for 0.32 and 0.45 mm I.D.; narrow bore column for 0.20, 0.25, and 0.28 mm I.D.; microbore column for 0.10, 0.15, and 0.18 mm I.D, as cited by Mastovska and Lehotay [2].

Fast chromatographic separations and, thus, short analysis times, have always been a requisite for new analytical methodologies. The increase in the analysis speed may be obtained through increased values of the optimal linear velocity, $\bar{u}_{opt}$. According to Van Deursen et al. [7], the following relation defines $\bar{u}_{opt}$ and includes the parameters which directly influence it:

$$\bar{u}_{opt} = 8\frac{\overline{D}_m}{d_c}\sqrt{\frac{3(1+k)^2}{11k^2+6k+1}} \qquad (1)$$

where $\overline{D}_m$ is the average diffusion coefficient of the analyte in the mobile phase, d_c is the capillary column diameter and k is the retention factor of the analyte.

Indeed, it can be seen that, for a given column, $\bar{u}_{opt}$ is directly proportional to $\overline{D}_m$. Higher values of $\overline{D}_m$ may be obtained through the following two possibilities:

a) a reduction in the carrier gas molecular weight (e.g. the use of hydrogen or helium instead of nitrogen as carrier gas);
b) the use of vacuum outlet short and wide columns having minimum required theoretical plates (N_{req}), i.e. when the absolute value of the column inlet pressure will be minimal

To illustrate the influence of the carrier gas molecular weight and of the outlet pressure, Figure 2 presents the measured theoretical plate height H vs. $\bar{u}$ for nitrogen and helium as carrier gases at atmospheric and vacuum outlet. As predicted, gas velocities at the corresponding minimum of the curves are higher with helium than with nitrogen, while the shift of the minimum is evident for higher gas velocities through the decrease of the column outlet pressure from atmospheric to vacuum.

Relation (1) shows that $\bar{u}_{opt}$ also depends on the diameter of the capillary column used, d_c. Under vacuum outlet conditions, short, megabore columns are the most suited to be used since the vacuum would extend across the whole column length, providing a higher analysis speed than the same column operated at atmospheric outlet pressures. In contrast, when narrow bore columns are operated at vacuum outlet conditions, only a fraction of the column length is operated at sub-ambient pressures. This means that the gain in speed for narrow bore columns with high theoretical plate numbers, operated under vacuum conditions, becomes less important [9].

It was practically showed that vacuum GC separations on short, megabore capillary columns (ID of 0.53 mm) with a restriction at the inlet allow carrier gas velocities of about 100 cm/s for helium, which is a factor of 10 higher compared to the use of a megabore capillary column under normal pressure [12]. Indeed, under such high speed conditions, the eluting peaks are very narrow and the peak measurement would become problematic due to the limited speed of data rate acquisition. However, the peaks that elute from a megabore capillary column operated under vacuum outlet conditions have peak widths which are not as low as in microbore fast GC and therefore the mass spectral acquisition rate is sufficient [12].

The use of short, megabore capillary columns combined with vacuum outlet may generate an increase of the pressure in the ion source of the MS system to a level exceeding the tolerable limit. If the pumping system of the MS system does have sufficient capacity to maintain pressure at an acceptable level, the pressure in the injector will decrease to sub-ambient values which may cause additional practical problems. The above mentioned possible problems may be avoided by using of a microbore precolumn (retention-gap or restriction, which may serve also as a guard column) which should be connected to the head of the mega-bore column. The flow is now restricted to an acceptable level, the injection system can operate at above-atmospheric pressures and low-pressure conditions would still prevail throughout the entire column [12, 13].

For a given column, the gain in speed of analysis (*G*) when vacuum outlet pressure conditions are used compared to atmospheric outlet pressure conditions can be calculated using the following relation [9]:

$$G = \frac{p_{i,opt,atm}^3 - 1}{\left(p_{i,opt,atm}^2 - 1\right)^{3/2}} \qquad (2)$$

where $p_{i,opt,atm}$ is the absolute inlet pressure (in bar) under optimal conditions at atmospheric outlet pressure (p_o = 1 bar).

The optimum absolute inlet pressure under vacuum outlet conditions $p_{i,opt,vac}$ expressed in bar can be found from:

$$p_{i,opt,vac}^2 = p_{i,opt,atm}^2 - 1 \qquad (3)$$

G is seen to increase with decreasing values of $p_{i,opt,atm}$ [11]. Since the largest gains are obtained for columns that have low optimal inlet pressures, vacuum outlet will be of particular interest for high permeability (open tubular) columns, with a large inner diameter and/or a short length.

The use of megabore columns can also provide another advantage compared to microbore capillary columns. Because the maximum sample capacity is proportional to d_c^3 (the volume of one theoretical plate), the sample loadability is largely increased when using megabore capillary columns. It might be also interesting to increase the sample loadability even more by increasing the film thickness. To describe the influence of the film-thickness on the efficiency of a GC separation, the following relation [7] may be used:

$$\frac{H_{\min}}{\bar{u}_{opt}} = \frac{C_{m,o}}{f_2}\left(\frac{18}{8} + \frac{3}{2}\frac{C_s f_2}{C_{m,o}}\right) \qquad (4)$$

in which $H_{\min}$ is the minimum plate height at optimum conditions, f_2 is the pressure correction factor, $C_{m,o}$ is the resistance to mass transfer in the mobile phase at the column outlet conditions and C_s is the resistance to mass transfer in the stationary phase.

The increase in the film thickness results in an increased resistance to mass transfer in the stationary phase, and at a certain film thickness, the influence of slow diffusion in the stationary phase on the plate height can no longer be neglected. In other words, for a high film thickness, the separation becomes less efficient and separation time increases. If a column is operated at vacuum outlet conditions, the stationary phase starts to contribute significantly to band-broadening at much lower thicknesses than in the case of atmospheric outlet operation.

Combining the relation (4) with definition relations for $C_{m,o}$ and C_s, the following relation [7] could be obtained:

$$\frac{H_{\min}}{\bar{u}_{opt}} = \left(\frac{3}{8}\frac{11k^2+6k+1}{24(k+1)^2}\frac{d_c^2 p_i}{p_1 D_{m,1}}\right) + \left(\frac{k}{(k+1)^2}\frac{d_f^2}{D_s}\right) \qquad (5)$$

where p_1 and $D_{m,1}$ are the pressure and diffusion coefficient at atmospheric conditions, D_s is the diffusion coefficient of the solute in the stationary phase and d_f is the thickness of the stationary phase film.

Therefore, the total analysis time can be calculated by combining the last equation together with the following relation:

$$t_R = \frac{H_{\min}}{\bar{u}_{opt}} N_{req}(1+k) \qquad (6)$$

By using these equations, it is possible to determine at which film thickness the negative influence of slow mass transfer in the stationary phase is larger than the positive influence of lower inlet pressures (Figure 3). It can be concluded that if a megabore capillary column of 10

m length is used, to take full advantage of the gain in speed when vacuum outlet conditions are used, the film-thickness should not exceed approximately 1.5 μm (Figure 3). Another consequence of performing separations in vacuum conditions is that the components are measured, identified and quantified at much lower temperatures compared to atmospheric pressure conditions.

There are also several limitations of LP-GC, basically from the instrumental point of view. However, once the optimal operating conditions and the suitable application fields have been found, it may prove to be a useful technique. The LP-GC technique presents a series of advantages, which will be subsequently described in the following sections as it opens the possibility of being applied in many other fields than in currently used.

3. LP- GC applications

During the last few years, the application of vacuum GC has been developed and optimised successfully for the rapid analysis of pesticides (Table 1) and several other groups of compounds, such as polycyclic aromatic hydrocarbons (PAHs), hydrocarbons and volatile organic compounds (benzene, toluene and xylene), volatile aromas and industrial pollutants (Table 2). This chapter briefly describes the main features of these applications, including details on the various column setups and MS systems used.

3.1 Pesticides

Mastovska et al. [14] explored the LP-GC technique for the analysis of 20 representative pesticides in vegetable samples (e.g. carrots). The performance of LP-GC was compared to a conventional RTX-5 Sil MS capillary column (30 m x 0.25 mm, d_f = 0.25 μm). They reported that, if no co-eluting interferences arose from matrix, the injection of 2 μL provided the lowest LODs for the deltamethrin, phosalone, procymidone, captan, pirimiphos-methyl, heptachlor, and propargite. However, for some pesticides, e.g. acephate, dimethoate, thiabendazole, and methiocarb, interferences were present using the LP-GC setup, but not in conventional GC, likely due the reduced separation efficiency. Typical chromatograms obtained for a mixture of pesticides by LP-GC and conventional GC is shown in Figure 4. Limited thermal degradation of thermally-labile analytes, such as carbamates, was also reported in LP-GC. Further, the authors proposed direct sample introduction in LP-GC as larger extract volumes could be injected without clean-up or solvent evaporation.

Gonzalez-Rodriguez et al. [15] have investigated the suitability of LP-GC combined with ion-trap tandem mass spectrometer (IT-MS/MS) to analyze a large number (n = 72) of

pesticide standards. Results were compared using a conventional capillary column (CP Sil 8 CB 30 m x 0.25 mm i.d., d_f = 0.25 μm). The total analysis time was significantly reduced in LP-GC (32 min) compared to conventional GC (72 min). The authors also observed a better precision and sensitivity using the LP-GC approach i.e. RSDs ranged between 3 - 17 % compared to 5 – 31 % obtained with conventional GC. The LODs for the multiclass pesticides ranged from 0.1 to 14.1 μg/L for LP-GC and were similar or lower than those obtained by conventional GC, range 0.1 to 17.5 μg/L. Figure 5 demonstrated this for pirimifos-methyl and bifenthrin. Furthermore, the peak widths obtained with the short wide-bore column in LP-GC were similar to those obtained using conventional GC column, while peaks could be successfully identified by MS/MS detection with the conventional scan speed of the ion-trap instruments.

The same research group has also applied LP-GC for the pesticide determination in agricultural plant waste from beans, watermelons and melons [16]. Since matrix effects on the analytical signal were noticed for most pesticides, the use of matrix-matched standards was recommended. Linearity, LODs, recovery and precision were calculated for each of the 70 multiclass pesticides. For all the three matrices, LOQs varied from 0.2 to 47.2 μg/L for lyophilized samples, except for propoxur and dimethoate. Good recoveries (70 - 130 %) were obtained with RSD values < 16 % for all pesticides. Vegetables grown without pesticides were used as blank samples.

Arrebola et al. [17] used LP-GC for the fast analysis of 72 pesticides in vegetables without clean-up. In comparison to other studies [14, 18], they have used large injection volume (10 μL) in a split/splitless injector using a liner which contained a plug of carbofrit. Interestingly, no carry-over effect was reported. In comparison to the conventional GC on a DB - 5MS column (30 m x0.25 mm I.D., 0 d_f = 0.25 μm), the analysis time was reduced by half and separation was completed in 31 min. The LOQ values ranged from 0.06 to 13 μg/kg except for disulfoton, which showed a higher value (22 μg/kg), while RSDs lower than 17 % were reported for all pesticides.

In an another study, Mastovska et al. [18] further evaluated and optimized the quadrupole LP-GC-MS for the routine analysis of 57 pesticide residues in food crop extracts. As shown in Table 2, two column combinations were tried and the narrower analytical column (0.25 mm i.d.) with a thinner film resulted in the faster analysis of various pesticides. However, no significant difference in precision of peak area and height measurement was observed for both columns showing that the analyte response was not affected by the matrix.

Further the study also highlighted the significance of ruggedness in routine analysis of real-world samples with fast GC approaches.

Pesticides in different types of processed (whole, skimmed and powdered) and unprocessed goat and human milk samples were determined by using solid-phase microextraction (SPME) and LP-GC-MS/MS [19]. After optimization, 40 multiclass pesticides were eluted in a reasonably short time of 26 min. Further, compared to conventional GC using a DB - 5MS column (30 m x 0.25 mm I.D., d_f = 0.25 µm), the elution of high boiling compounds was possible by LP-GC, while the elution of thermally-labile compounds was possible at lower temperatures (lower by 30-60 °C). This minimized the bleed of the analytical column due to lower elution temperature, which in turn resulted in a higher sensitivity. The authors also founded that the above column combination reduces potential milk interferences (from fats and protein). The LOQs ranged from 0.02 to 1.0 µg/L and RSD were < 20 %.

A LP-GC method was developed and validated for the multiclass pesticide residue in compost to avoid environmental contamination and to assure worker safety [20]. Pesticide residues were extracted from lyophilized samples with organic solvent by stirring and no post-extraction clean-up was performed before analysis. The recoveries were between 72 and 109 % and RSDs were always < 12 %. The LOQ for lindane, malathion, chlorpyrifos-methyl and endosulfan were 4.2, 3.9, 14.9 and 12.8 µg/L, respectively. The authors concluded that the proposed LP-GC methodology was reliable for the analysis of compost samples.

Walorczyk and Gnusowski [21] studied the feasibility of LP-GC in conjunction with a triple quadrupole MS/MS as a route towards fast analysis of pesticide residues. The analysis time compared to a conventional RTX-5 (30 m x 0.25 mm, d_f = 0.5 µm) was greatly reduced using a LP-GC column (i.e from 37 min to 13 min). Furthermore, the rate of false negative results was also reduced with LP-GC, while peaks were improved in both size and shape enabling thus correct identification of pesticides at lower levels. The average recoveries obtained were 103 % and 102 % for the conventional GC and LP-GC, respectively. Further, the authors mentioned that the conventional GC-MS failed to determine iprodione at 0.2 mg/kg, whereas the LP-GC provided recoveries of 93 %, 96 % and 102 % in full scan, SIM and MS-MS mode, respectively. The authors also suggested that LP-GC based methods (especially those using highly sensitive and specific MS/MS detection) are of practical value in application areas requiring reliable determination at very low concentration levels, such as analysis of pesticides in baby foods.

Fernandez-Moreno et al. [22] analysed 65 pesticide residues in fatty vegetables (e.g. avocado) based on clean-up by gel permeation chromatography and LP-GC, elution being completed in 31 min. LOQs ranged from 0.1 to 8.3 µg/kg, with the majority being less than 2.5 µg/kg. Acceptable recoveries were obtained for all pesticides with the precision values < 19 %. The successive injection of avocado extracts did not caused any damage to the chromatographic signal and no peak tailing was observed. The authors suggested LP-GC as a useful tool for the analysis of fatty matrices when a preliminary clean step is carried out.

3.2 Polycyclic aromatic hydrocarbons (PAHs) and other hydrocarbons

Ravindra et al. [27, 27b] developed a fast method for the determination of PAHs using LP-GC and pressurized liquid extraction (PLE). In comparison with conventional CP Sil 8 column (30 m x 0.32 mm, d_f = 1.0 µm), the application of LP-GC allowed a three-fold reduction in the analysis time with the preservation of the chromatographic resolution for low-molecular weight (MW) PAHs and improved detection limits. However, they also reported a loss of separation power for high MW PAHs. Except for some PAHs, the LODs were in the same range (65 to 150 pg) for both GC setups and a RSD < 15 % was reported. Further, the peak width at half height of 1.5 s matched the ITMS duty cycle. The LP-GC technique was applied for the analysis of vapour and aerosol phase PAHs in air samples collected near a highway and in aerosol samples from sugar cane burning [26].

The rapid determination of B(a)P in olive oil samples was achieved using solid-phase extraction and LP-GC-MS conditions [28]. The analysis time was only 8 min in comparison to 42 min using conventional GC on a DB - 5MS column (30 m x 0.25 mm I.D., d_f = 0.25 µm). However, the LOD was slightly higher (1.6 µg/kg) for LP-GC compared to conventional GC (1.0 µg/kg) or HPLC (0.5 µg/kg) with recoveries above 80% in all cases. The method was also applied to routine analysis and found to be economically viable as it allows handing of 50-100 samples in one working day. The authors suggested that the LP-GC method may also be applied for other PAHs as well as for other edible oils.

De Zeeuw et al. [12] have shown the application of LP-GC for C_9 to C_{18} compounds. The separation was achieved in less than 6 min using a CP-Sil 8CB (10 m x 0.53 mm) with restriction column. Further, they also found that C_{70} hydrocarbons eluted in about 32 min and up to C_{80} hydrocarbons could be eluted under vacuum conditions. The theoretical plate number was reduced by 30 - 40 % compared to standard GC methods. Furthermore, the C_9 compounds were found to have a peak width of 1.7 s and matched the IT-MS duty cycle for quantitative analysis.

3.3 Volatile organic compounds (VOCs)

Joos et al. [25] described a rapid determination of benzene, toluene, ethylbenzene and three xylene isomers, including a nearly baseline separation of the xylene isomers in air samples within 1 min using LP-GC-ITMS. As shown in Table 2, different columns and lengths were studies. A LP-GC ChiraSil Dex column was found to be the most suitable and retention times were reduced from 8 min to 1 min, compared to a CP Wax 52 column (10 m x 0.53 mm, d_f = 1.0 µm). Further, a column length of 10 m instead of 15 m for the megabore column was also suggested. A precision of 5 - 17 % was obtained and LODs of the investigated VOCs in air were approximately 0.01 µg/m^3 using diffusive samplers.

3.4. Plant/Flower oils

Many species of the genus Turnera (*turneraceae*), such as *Turnera diffusa*, are widely used in phyto-pharmaceutical formulations. Godoi et al. [24] has proposed LP-GC-ITMS as a potential tool for the quality control of essential oils (e.g 1,8-cineole or thymol). These compounds were analysed in significantly less time using LP-GC column compared to conventional GC (LM-5 column, 15 m x 0.2 mm; d_f = 0.25 µm). However, it has to be noticed that both column had different stationary phase. The RSD were ~ 7 % for 1,8-cineole and 5 % for thymol. Further, the authors also claim that the identification capabilities for other components of the essential oils remain at the same levels as in the conventional GC system described above.

Mena Granero et al. [23] also coupled the headspace solid-phase microextraction (HS-SPME) and LP-GC–MS-MS for determination of 20 volatile compounds present in *Cucurbita pepe* flowers. These compounds included benzene, toluene, ethylbenzene, m-xylene, p-xylene, o-xylene, α-(+)-pinene, myrcene, R-(+)-limonene, eucalyptol, ocimene, linacolool, 1,4-dimethoxybenzene, p-anisaldehyde, cinnamaldehyde, indole, cinnamyl alcohol, dibutyl phthalate, eugenol, and 1,2,4-trimethoxybenzene and were analysed in 26 min. Lower LOQs were reported than for conventional GC and ranged from 2 to 10 ng with the majority being lower than 6 ng with recoveries of 95- 103 % and RSDs < 17 % for all compounds.

3.5. Organotin compounds

Eight organotin compounds (i.e. monobutytin, dibutyltin, tributyltin, tetrabutyltin, monophenyltin, diphenyltin, triphenyltin and tetraphenyltin) were determined in water, sediments and mussels by LP-GC-MS-MS method [29]. Solid-phase extraction was used as

extraction method from water samples after comparison with liquid–liquid extraction, but extraction of organotins from sediment and mussels was performed using toluene. Matrix-matched calibration standards were used to minimize matrix effects. The implementation of LPGC rather than conventional capillary GC permitted use of large-volume injection and reduced analysis time by a factor of two. The recoveries were > 80%, with precision values < 18% for all organotin compounds in all medias. The LOQ values ranged from 0.4-32 ng/L, 0.22-2.51 µg/kg and 0.11-16.6 µg/kg for water, sediments and mussels, respectively.

3.6. Steroid estrogens

A wide range of estrogenic contaminants has been detected in the aquatic environment. Hajkova et al. [30] have recently developed and validated a LP-GC method for the direct analysis of estrone, 17β-estradiol, 17α-ethinylestradiol, dienestrol, and diethylstilbestrol in river sediments. These natural and synthetic steroid estrogens are typically present in municipal sewage treatment plant effluents are the most persuasive. Relatively low LODs (1.5 - 5 ng/g dried sediment) and good repeatability of GC splitless injection (RSD 1 – 2 %) were achieved with LP-GC with a single quadrupole MS. The results were also compared using a DB-17 MS column (30 m x 0.25 mm id, d_f =0.15 µm) and it was found that LP-GC is a suitable option for routine analysis, not only because of rapid separation of sample components at low temperatures, but also due to its lower LODs compared to a conventional GC system. Indeed, the total analysis time for conventional capillary GC was 14.6 min, while only 7.6 min were needed for the LP-GC technique.

3.7. Polybrominated diphenyl ethers (PBDEs)

Based on the ability of LP-GC to elute compounds at lower temperatures [12], the applicability of LP-GC–MS operated in electron-capture negative ionization mode (ECNI) for the analysis of decabrominated diphenyl ether (BDE 209) was reported [31]. This congener was found of particular interest because of its thermal degradation in conventional GC systems when elution temperatures above 300 °C or high residence times in the column are applied. By using LP-GC, an elution temperature of 295 °C combined with very short residence times at the maximum oven temperature were achieved, obtaining thus minimal thermal degradation of BDE 209. Furthermore, baseline separation of 22 major PBDE congeners was also achieved in less than 12 min using the column with d_f = 0.15 µm. The authors have also assessed the feasibility of LP-GC for the quantitative analysis of PBDEs in Belgium indoor dust samples and found it suitable for routine analysis.

In two other studies, baseline separation of 8 PBDE congeners, including BDE 209, was achieved in 20 min using a 10 m x 0.53 mm, d_f = 0.15 μm CP-Sil 8 wide-bode column [34, 35]. In both cases, the authors have demonstrated the utility of MS-MS analysers to lower the background and obtain thus low LODs. However, these studies have not demonstrated the applicability of LP-GC to real samples.

3.8. Polychlorinated biphenyls (PCBs) and other semi-volatile compounds (sVOC)

The usefulness of LP-GC coupled with time-of-flight mass spectrometry (TOFMS) was investigated by Cochran et al. [32]. The analysis time was reduced from 10.5 to 4.25 min with LP-GC column (Table 2) in comparison to conventional DB - XLB column (40m x 0.10mm, d_f = 0.10 μm). However, co-elution between congeners belonging to the same homologues group occurred. The authors suggest that this setup may be useful for determination of Aroclor mixtures in capacitor fluids or Aroclor spills, in which congener specific measurement are not necessary. Interestingly, very narrow peak widths (1.5 s at the base) were obtained with LP-GC, probably due to high diffusion coefficients.

Cochran [32] applied the LP-GC-TOFMS also for the analysis of 145 semivolatile compounds having differences in their mass spectra (pesticides, phenols, PAHs, phthalates, nitro-derivatives, etc). He found that TOFMS offers a powerful alternative to the co-elution problem and allows fast analysis with LP-GC (total analysis time was 4.25 min). Furthermore, peak-find and deconvolution algorithms built around the acquisition speed and spectral reproducibility of TOFMS may offer another separation dimensions and produce library-searchable mass spectra.

4. Advantages and limitations of using LP-GC

As it was suggested above, there are some advantages of using LP-GC technique which will be described point by point in the following section.

Firstly, using increased velocities and a shorter column, a reduction in the analysis time by a factor of 3-7 or 10 in the case of temperature-programmed or isothermal elution, respectively, is possible.

Further, the LP-GC technique allows analytes to elute at much lower temperatures; elution temperatures can be with 30-60 °C lower [12], this being beneficial for the analysis of thermally-labile compounds. These two important mentioned advantages can be translated practically into the possibility of applying LP-GC in two situations: elution in a shorter time of a certain mixture of compounds which applying the conventional GC methods would take a

longer separation time or, using the same elution time as in conventional GC methods, compounds with higher elution temperatures may be also analyzed.

Other attractive features of LP-GC are:

a) It is compatible with existing injection techniques and mass spectrometer analyzers;
b) The improvement in the peak shape in LP-GC will result in a higher sensitivity and thus an improvement of typically 2-5 fold in the limits of detection;
c) Lower elution temperatures of target analytes, which results in lower signal intensity of the column bleed and less interferences with masses of the target analytes. LP-GC allows the elution of higher boiling compounds and of thermally labile compounds at lower temperatures (lower by 50–80 ^{o}C).
d) High sample loadability; the 0.53 mm megabore column can provide high loadability as films up to 5 µm can be deposited [2]. High sample loadability makes overloading very difficult, which is of particular interest if traces have to be analyzed. Furthermore, Gonzalez-Rodriguez et al. [19] found that LP-GC also reduces potential interferences due to high sample capacity of the column.
e) Megabore columns (0.53 mm i.d.) can take more stress than microbore capillaries;
f) Thermal degradation of labile analytes is reduced.
g) The LP-GC setup is commercially available as Rapid-MS^{TM} from Varian.

Despite the attractive speed and loadability characteristics of mega-bore columns operated under vacuum outlet conditions, the LP-GC approach is hampered by several experimental difficulties. As mentioned before, the high column outlet flow might increase the pressure in the ion source of the mass spectrometer to a level exceeding the tolerable limit. Typical optimum column outlet flow-rates of a mega-bore column (10 m x 0.53 mm I.D.) are approximately 7-10 mL/min. In general, the maximum pumping capacity of MS is already reached at a column flow-rate of 5 mL/min [13]. Furthermore, an excessive pressure in the ion source can lead to damaging/burning of the filament, especially when chemical ionization is used. However, non-MS applications of LP-GC are inconvenient since the column setup is operated at atmospheric pressure outlet. Further, the efficiency of capillary columns operated at low pressure is lower. The number of theoretical plates will be lower for LP-GC column, compared to the conventional columns as discussed above [12, 27]. However, the loss in theoretical plates is an acceptable shortcoming, when the increased sample throughput is taken into account.

5. Practical approaches of using LP-GC

When applying LP-GC, no significant changes in the instrumental setup are needed, but there are few practical issues which need to be considered:

1. Length of the micro-bore restriction. Since the restriction is responsible for the inlet pressure, care has to be taken that this part of the LP-GC column setup does not operate under sub-atmospheric conditions. Optimum lengths are between 0.5 and 1 m for 0.1 mm ID and between 1 and 3 m for 0.15 mm I.D.
2. The chosen injection technique has to be compatible with the restriction. This means that on-column injection is less suitable when micro-bore restrictions are used.
3. Oven temperature. Depending on the number of analytes which has to be analyzed by LP-GC, the oven temperature can be programmed in such way that the analysis time is shortened. Oven rates up to 60 °C/min can be used [24, 26]. However, typical rates are between 20 and 30 °C/min.
4. Film thickness. While thick films favour higher sample capacity, it will also increase the retention time of the analytes. On the contrary, thin films will lead to short retention times, but lower sample capacity. Figure 3 shows that theoretically it was proven that if a megabore capillary column of 10 m length is used, the film-thickness should not exceed approximately 1.5 μm in order to take full advantage of the gain in speed when vacuum outlet conditions are used [7].
5. Separation efficiency. There is a substantial loss in the number of theoretical plates for LP-GC and consequently, in the separation efficiency i.e. the number of theoretical plates will be about 30-40 % lower compared with the theoretical plate number under conditions with atmospheric outlet [12].
6. Matrix effects. Because of higher sample capacity, mega-bore columns (0.53 mm i.d.) are preferred to 0.32 mm I.D. columns with regards to matrix effects.

It was mentioned above that, due to use of mega-bore column, relatively broad peaks with typical peak width at half peak of 1.5-2 s are obtained, what make possible the use of conventional ion-trap (IT) or quadrupole analyzers (Figure 6). Single quadrupoles are the most widely used mass analyzers and have a relatively low cost and established engineering. However, an ion-trap has the MS/MS advantage that is very important for fast GC/MS, especially with target compound analysis. Both analyzers can be operated at relatively high pressure making them compatible with high flow rates used in the wide-bore column. In addition, due to the short column and high flow rates, sharp peak are obtained for LP-GC,

while the S/N ratio improves significantly, which results in lower LODs compared to conventional GC (Table 3).

6. Prospects of LP-GC

In the above sections, one has seen the various development and application of LP-GC. Despite the attractive features discussed in section 3, only few application of LP-GC appeared in section 4. Therefore, there is still a potential to further develop LP-GC for various other compounds, such as:

a) Compounds which are thermally-labile as the use of LP-GC lead to lower elution temperatures than in conventional GC.
b) Food-related compounds, such as additives, flavour and aroma components, but also natural toxins, veterinary drugs and packaging materials as suggested by Lehotay and Hajslova [35]. Further, the LP-GC application with high resolution and high-speed TOFMS analysers offer potential not only for target, but also for non-target analysis of a wide range of semivolatile organic compounds present in food and other matrices [32, 33].
c) Fast identification and analysis of key compounds for industrial, environmental, medical and forensic applications.

7. Conclusions

These above reviewed studies related to the application of LP-GC for the determination of various compounds revealed that LP-GC with short megabore column provides equal or improved analytical figures compared to conventional GC. However, the list of investigated compounds is still short and hence in the near future, the application of LP-GC for the analysis of other compounds is expected. Fields of interest might include industrial, environmental, food, medical of forensic applications.

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Table 1. Recent applications of low pressure-gas chromatography in pesticide analysis.

Matrix	Restriction	LP-GC Column	Analyzer	Remarks	Gain in retention time[a]	Reference
Vegetables	fused silica (3m x 0.15mm)	RTX-5 Sil (10m x 0.53mm x 1.0μm)	Q	LODs were not limited by matrix interferences	< 3	[14]
Standard solution	Fused silica (0.6m x 0.10mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	IT	Method optimization, Lower LODs	< 2.5	[15]
Post-harvest plants/animal feed	Fused silica (2m x 0.25mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	IT	-	< 2	[16]
Vegetables	fused silica (2m x 0.25mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	QqQ	Samples analyzed without clean-up	< 2	[17]
Food crops	fused silica (3m x 0.15mm)	RTX-5 Sil (10m x 0.53mm x 1.0μm) DB-5 (10m x 0.25mm x 0.25μm)	Q	Ruggedness was tested for routine analysis	< 3	[18]
Milk (processed and unprocessed)	fused silica (0.6m x 0.10mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	IT	Reduced fat interference	< 2	[19]
Composts	Fused silica (0.6m x 0.10mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	IT	Samples analyzed without clean-up	< 2	[20]
Vegetables	fused silica (2.5m x 0.15mm)	HP 5 (10m x 0.32mm x 0.25μm)	QqQ	Lower LODs	< 3	[21]
Fat vegetable matrices (avocado)	fused silica (0.6m x 0.10mm)	CP Sil 8CB (10m x 0.53mm x 0.25μm)	IT	No peak tailing for fatty matrices	n.a.	[22]

[a] - compared to conventional GC; n.a. – not available; MS analyzers: Q - quadrupole, IT - ion trap, QqQ - triple quadrupole

Table 2. Recent applications of low pressure-gas chromatograhy for various classes of compounds.

Compounds	**Restriction**	**LP-GC Column**	**Analyzer**	**Remarks**	**Gain in retention time[a]**	**Reference**
Volatile compounds in *Cucurbita* Flower*	fused silica (2m x 0.25mm)	CP-Sil 8 (10m x 0.53mm x 0.25µm)	IT	Coupled HS-SPME and LP-GC, analysis time 26 min	n.a.	[23]
Turnera Diffusa (ward.) oil	fused silica (1.0m x 0.10mm)	CP Wax 52 (10m x 0.53mm x 1.0µm)	IT	Analysis time 3 min	< 7[†]	[24]
VOCs (benzene, toluene and xylene isomers)	fused silica (1.0m x 0.10mm)	CP Wax 52 & 57 (10m x 0.53mm x 1.0µm); CP Wax 52 (10m x 0.53mm x 2.0µm); ChiralSil Dex (10m x 0.53mm x 1.0µm)	IT	Use of ChiralSil Dex suggested	< 7[†]	[25]
PAHs (16 US EPA)	fused silica (1.0m x 0.10mm)	CP Sil 8 (10m x 0.53mm x 1.0µm)	IT	Analysis time 13 min	< 3	[26]
PAHs (18 US EPA)	fused silica (1.0m x 0.10mm)	CP Sil 8 (10m x 0.53mm x 0.25µm)	IT	baseline separation of low MW PAHs	< 3	[27]
B(a)P	fused silica (0.6m x 0.25mm)	CP-Sil 8 (10m x 0.53mm x 0.50µm)	Q	Broad peak of B(a)P	< 5	[28]
Organotin compounds*	fused silica (0.6m x 0.10mm)	CP-Sil 8 CP (10m x 0.53mm x 0.25µm)	QqQ	Used also a guard column, analysis time 12.5 min	< 2	[29]
Steroid estrogens	fused silica (5.0m x 0.18mm)	RTX-5 Sil (9m x 0.53mm x 0.5µm)	Q	Low LODs and RSDs	< 2	[30]
Polybrominated diphenyl ethers	fused silica (1.0m x 0.10mm)	AT-5 (10m x 0.53mm x 0.10µm) CP-Sil 8 (10m x 0.53mm x 0.25µm)	Q	Baseline separation of 22 PBDE congeners, including BDE 209	< 2	[31]
PCBs in an Aroclor mix and in sediments	fused silica (3m x 0.18mm)	CP-Sil 8 CB (5m x 0.53mm x 0.5µm)	TOF	145 semivolatile compounds could be analysed with the same method	< 2	[32]

* see text for more details; ** - compared to conventional GC; n.a. – not available; MS analyzers: Q - quadrupole, IT - ion trap, QqQ - triple quadrupole; TOF – time of flight; [†] Column with different stationary phase were compared.

Table 3. Comparative analytical parameters between LP-GC and conventional GC for selective compounds.

Sample	Compounds	LP-GC		Conventional GC		Reference
		LOD (µg/kg)	RSD (%)	LOD (µg/kg)	RSD (%)	
air	PAHs	50-140[a]	5-15	65-120	-	[27]
fresh fruits, vegetables	pesticides	0.1-0.6	2.1-5.5	0.2-4.4	0.0-12	[21]
carrot extracts	20 pesticides	0.3-203[b]	-	0.1-35	-	[14]
pesticide mixtures	72 pesticides	0.1-14.1[c]	5.5-23.1	0.1-17.5	4.0-30.8	[15]
indoor dust	PBDEs	0.02-0.11	< 4.8	0.03-0.09	< 7.4	[31]
olive oil	benzo(a)pyrene	1.6	-	1.0	-	[28]
sediments	steroid estrogens	1.5-5	1-2	1.5-5	6-12	[30]

[a] – reported as pg injected
[b] – injections of 1 µL carrot extracts
[c] – injections of 5 µL of standard mixture of pesticides (expressed as ng/mL)

Figure 1: Vacuum separation by applying a restriction column at the injection side of the system.

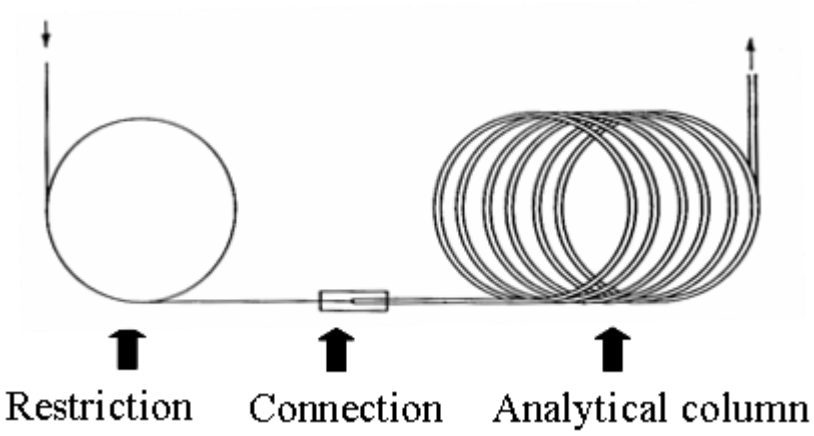

Figure 2: Measured H vs. $\bar{u}$ curves with nitrogen (a) and helium (b) as carrier gases at atmospheric and vacuum outlet (solute: *n*-dodecane tuned to k = 2 by adjusting T_c. Columns: 0.38 mm ID SE-30; "thin": L=30 m, d_f=0.4 μm, T_c=127 ^oC; "normal": L=34 m, d_f=1 μm, T_c =149^oC). Reproduced with permission from reference [9].

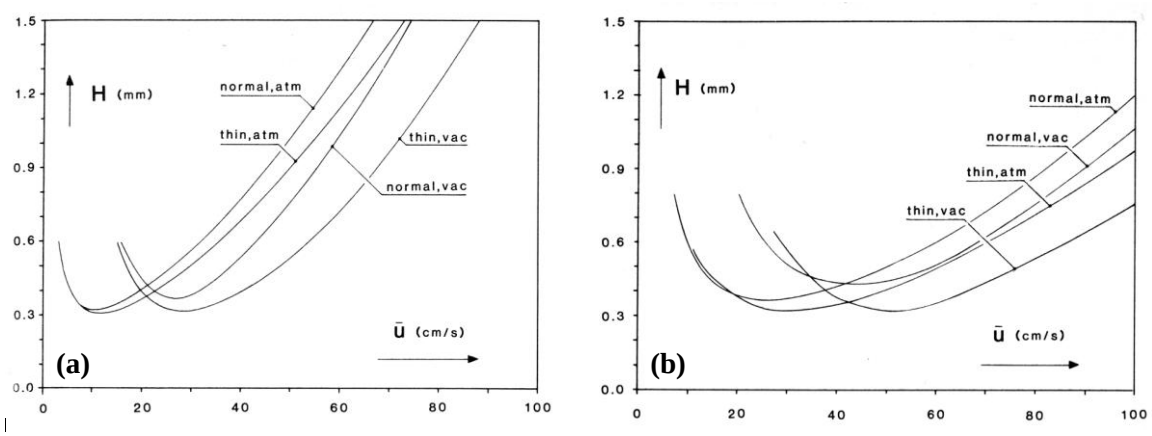

Figure 3: Influence of the film-thickness in a wide-bore column (10 m X 530 μm) on the analysis time. Drawn line: total retention time; dotted line (large): influence stationary phase on analysis time; dotted line (small): influence diffusion in mobile phase on analysis time. Plate-number: 20,000, compound: nonane, T = 60 ^{o}C, detector: mass spectrometer. Reproduced with permission from reference [7].

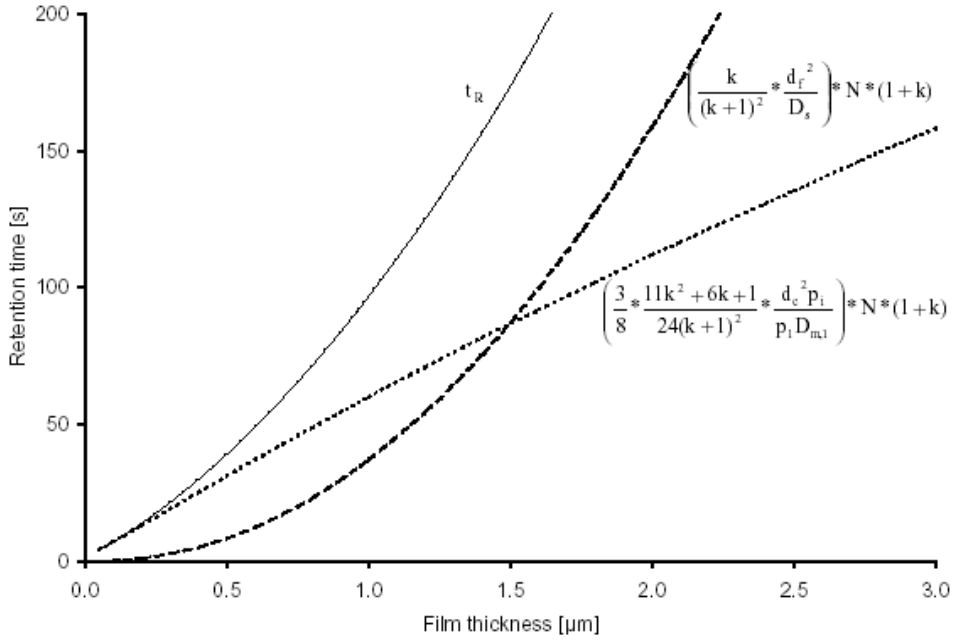

Figure 4. Typical chromatogram of a pesticide mixture (5 ng in toluene) at: (A) the optimized LP-GC–MS conditions, (B) conventional GC–MS conditions. Peak identification: (1) methamidophos, (2) dichlorvos, (3) acephate, (4) dimethoate, (5) lindane, (6) carbaryl, (7) heptachlor, (8) pirimiphos-methyl, (9) methiocarb, (10) chlorpyrifos, (11) captan, (12) thiabendazole, (13) procymidone, (14) endosulfan I, (15) endosulfan II, (16) endosulfan sulfate, (17) propargite, (18) phosalone, (19) *cis*-permethrin, (20) *trans*-permethrin, (21) deltamethrin. Reproduced with permission from Mastovska et al. [14].

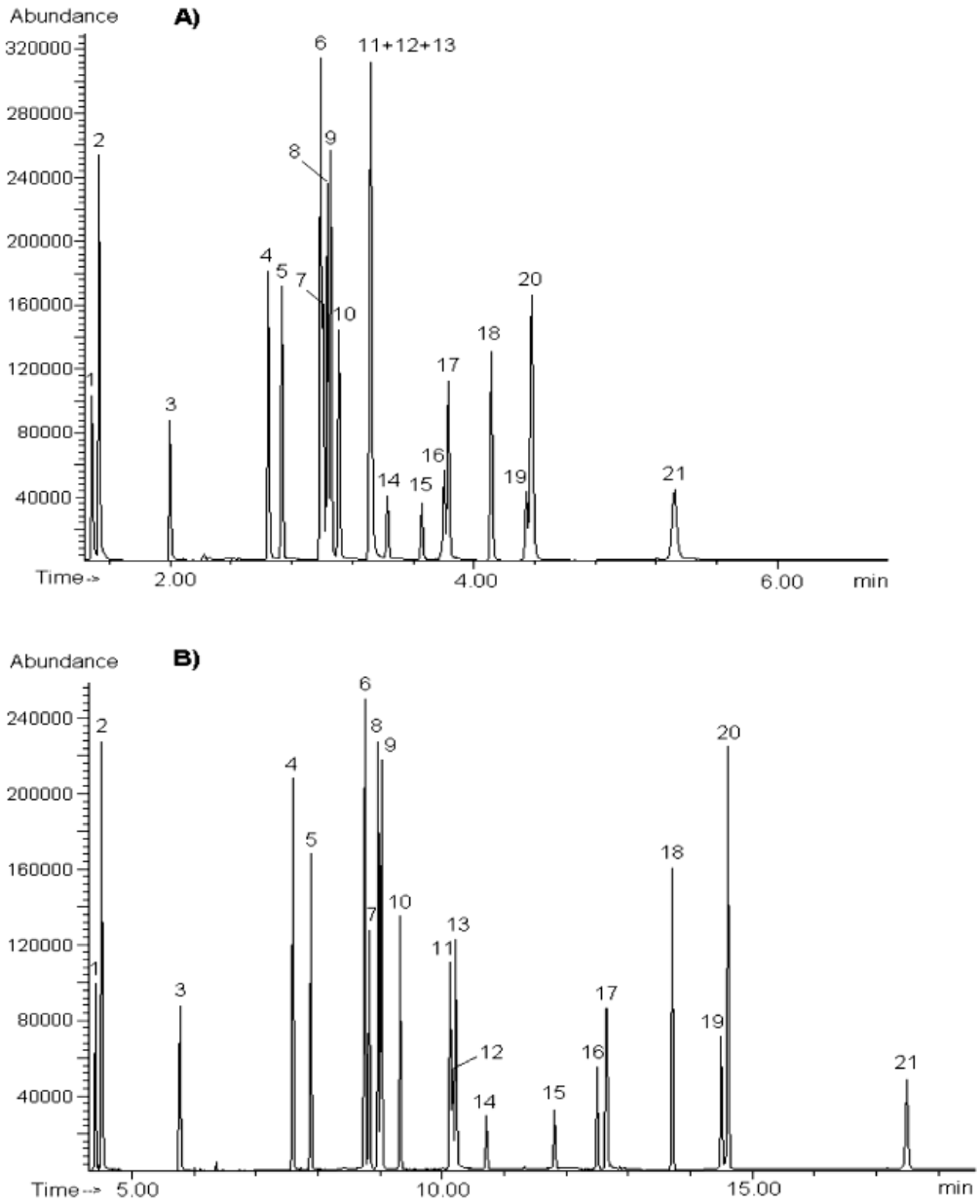

Figure 5. Elution profiles of 500 µg/L of pirimifos-methyl using LP-GC (retention time 8.31 min) and conventional GC (retention time 19.35 min) (a) and elution profiles of 50 µg/L of bifenthrin by LP-GC (retention time 18.44 min) and conventional GC (retention time 49.53 min) (b). Reproduced with permission from Gonzalez-Rodriguez et al. [15].

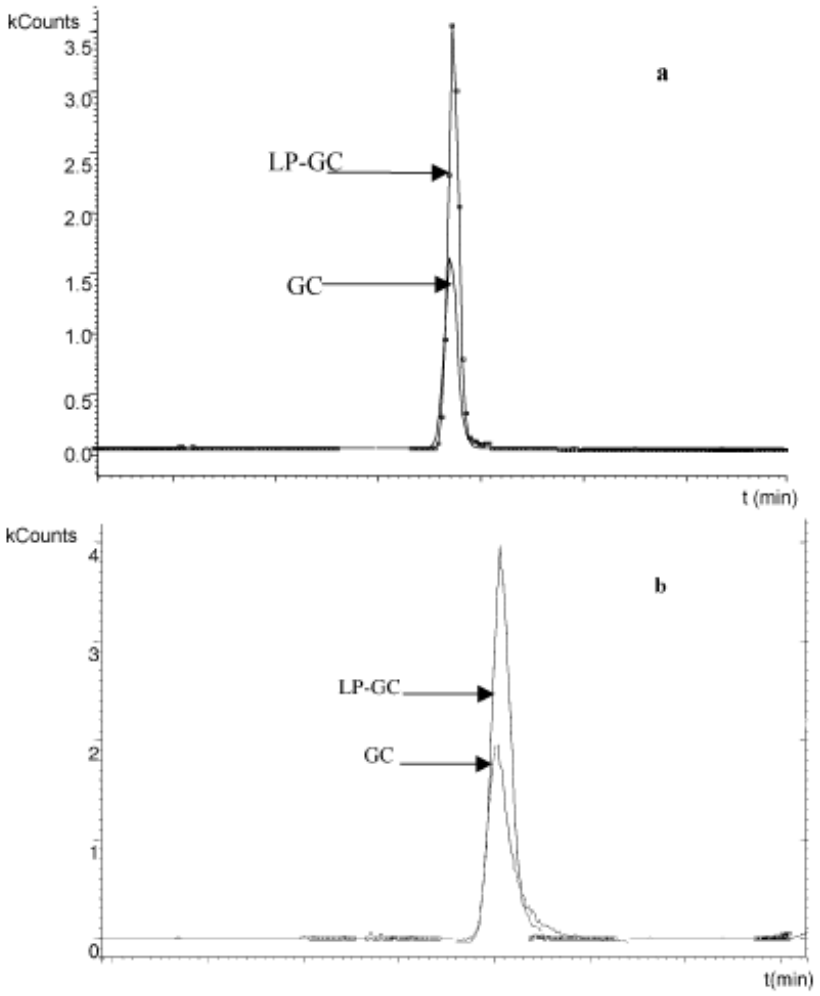

Figure 6. Comparison of peak shapes of thiabendazole (*m*/*z* = 201) and procymidone (*m*/*z* = 283) obtained for the injection of 1 µl (concentration 250 pg/µl) on a (A) conventional GC–MS (30m x 25 mm I.D., d_f = 0.25 µm RTX-5 Sil MS) and (B) LP-GC–MS (10 m x 53 mm I.D. d_f = 1 µm RTX-5 Sil MS). Reproduced with permission from Mastovska et al. [14].