

Review

Determination of gas–liquid partition coefficients by gas chromatography

Reynaldo César Castells^{a,b,*}

^a *División de Química Analítica, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, 47 esq. 115, 1900 La Plata, Argentina*

^b *CIDEPINT, La Plata, Argentina*

Abstract

This review covers theoretical principles and experimental procedures for the determination of gas–liquid partition coefficients, K_L , by gas chromatography. In order to precisely define the relationship between K_L , retention time and experimental parameters, the retention theory, both for ideal and for imperfect gas phase, is expounded. The most important sources of systematic error, as peak asymmetry, mixed retention mechanisms, column hold-up time and stationary phase mass determination, are discussed. Although the review is focussed on packed columns, comparison to capillary columns is discussed in those aspects in which these last show advantages.

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1. Introduction

The gas–liquid partition coefficient for the equilibrium distribution of a volatile solute between a vapor and a liquid phase is defined by the relationship:

$$K_L = \frac{C_L}{C_M} \quad (1)$$

where C_L and C_M represent the equilibrium solute concentration in the liquid and in the vapor phase, respectively. K_L

is of paramount importance in solution thermodynamics and an essential term in the retention equations of gas–liquid chromatography (GLC). It can be calculated from retention measurements, a fact that was soon perceived and exploited by chromatographers: Bradford et al. [1] were the first authors to report a gas chromatographically measured K_L as early as in 1955.

The theoretical foundations and the experimental procedures for the accurate measurement of partition coefficients were set up during the 1960s and 1970s by a relatively small number of distinguished chromatographers. Hundreds of papers reporting K_L values for a great diversity of solutes and solvents have been published since then. It is a matter of

* Fax: +54-221-427-1537.

E-mail address: rcastell@quimica.unlp.edu.ar (R.C. Castells).

concern that correct measuring procedures have not always been followed and, even more, that the number of papers rejected by referees in this area has increased in recent years. In order to remedy this state of things the Editor of the present special issue considered that a review article covering theoretical and practical aspects of the accurate measurement of gas–liquid partition coefficients would be pertinent and of value. A comprehensive treatment can be consulted in two recognized monographies [2,3] that, notwithstanding the time passed since their publication, remain as works of reference.

Plots of C_L against C_M may be concave or convex at moderate concentrations; however all isotherms become linear at sufficiently low concentrations. The linear region, characterized by a constant K_L , is known as the Henry's law or infinite dilution region. Both theoretically and experimentally GLC is simpler at infinite dilution. Conder and Purnell [4] have extended the theory to finite solute concentration; however, measurements at finite concentration have not been so popular as those at infinite dilution, probably because under those conditions GLC loses much of the instrumental simplicity that constitutes its principal appeal. Consequently, the present review shall be restricted to infinite dilution measurements.

Another restriction of this review is referred to type of column. Capillary columns have been scarcely employed for the measurement of gas–liquid partition coefficients, mainly because the solvents that the people wish to study cannot be immobilized on the capillary walls. Thus, although almost all contemporary separations are performed in capillary columns, a significant amount of work with thermodynamic objectives is still done on packed columns. It is to packed columns that this review is devoted, with only minor references to work on capillaries. However, an important increase in the use of capillary columns for thermodynamical measurements is predictable for the next years due to the reasons given in Section 6; this subject is covered in detail in a separate paper of this review issue [5].

2. Retention theory

We shall start by considering a column cross section at a distance x from the column inlet and a time t after solute injection. Both because of packing irregularities and of parabolic flow profiles within the channels the flow rate is not homogeneous; with u we represent the surface-average linear rate of the carrier gas molecules at the cross section. The migration of solute molecules along the column consists in a sequence of phase transfers; as movement occurs only when the molecules are in the mobile phase, their surface-average linear rate of travel shall be equal to u times the fraction of the molecules in the mobile phase:

$$\frac{dx}{dt} = u \frac{C_M a_M}{C_M a_M + C_L a_L} = \frac{F}{a_M + K_L a_L} \quad (2)$$

where a_L and a_M are the stationary phase and the mobile phase cross sectional areas and $F = u a_M$ is the carrier gas volumetric flow rate at x .

Zone migration, thus, is controlled by K_L , an equilibrium parameter. Of course, not all the zone migrates at equilibrium conditions: some of the molecules advance at a velocity higher than the equilibrium velocity, while others advance at lower velocities, this constituting the molecular origin of zone spreading; in the words of Giddings, "... equilibrium occurs at the zone center and nowhere else" [6]. At infinite dilution this process originates a symmetrical peak, with Eq. (2) giving the velocity of the peak maximum and, since K_L is independent of solute concentration, the velocity of the peak maximum is sample size independent. Therefore, symmetrical peaks and sample size independent retention times are characteristic of infinite dilution.

When solute concentration exceeds the infinite dilution region K_L becomes a function of concentration. When the isotherm is concave to the C_M axis K_L shall be a minimum at the peak maximum; in accordance with Eq. (2) molecules at the maximum shall be faster than those at lower concentrations, and consequently the zone shall advance along the column as a fronting peak that, on elution, produces a tailing chromatogram; the peak maximum retention time decreases as the sample size increases. Opposite effects (chromatograms with fronting peaks, with the retention times of their maxima increasing with sample size) are observed for isotherms that are convex to the C_M axis. Unlike infinite dilution peaks, asymmetrical peaks are not related to a single value of K_L ; values of K_L corresponding to different concentrations of solute in the mobile phase (i.e. an isotherm) can be obtained, after correcting for zone spreading, by analyzing the retention times at the diffuse side of the peak by methods developed for finite concentration chromatography [4].

A pressure gradient must be applied in order to overcome the flow resistance of the column. Since the mobile phase is a compressible fluid, the volumetric flow rate shall increase from a value F_i at the column inlet to a value F_o at the outlet. Integration of Eq. (2) in gas chromatography must take this into consideration.

2.1. Basic retention theory

Two assumptions are made by the simplest model: (a) the gas phase behaves ideally and (b) K_L is pressure independent. We are tempted to think that (b) is a consequence of (a); however, rigorous thermodynamic treatments indicate that it is not strictly so.

At constant mass flow rate, in accordance with assumption (a),

$$F_o p_o = F_i p_i = F p \quad (3)$$

or, since a_M is constant along the column,

$$u_o p_o = u_i p_i = u p \quad (4)$$

The relation between u and pressure gradient is given by Darcy's law [7]:

$$u = -\frac{B_o}{\varepsilon\eta} \frac{dp}{dx} \quad (5)$$

where B_o is the column specific permeability, ε the bed porosity and η represents the gas viscosity. Integrating Eq. (5) between inlet and outlet conditions leads to the result:

$$\frac{dx}{L} = \frac{-2p}{p_i^2 - p_o^2} dp \quad (6)$$

F and dx in Eq. (2) can be substituted by means of Eqs. (3) and (6), respectively, to give:

$$F_o dt = \frac{-2(V_M + K_L V_L)}{p_o(p_i^2 - p_o^2)} p^2 dp \quad (7)$$

with $V_M = La_M$ and $V_L = La_l$ representing the interstitial (void) and liquid phase volumes in the column. Eq. (2) can now be integrated between the limits $\{t = 0, p = p_i\}$ (corresponding to solute injection) and $\{t = t_R, p = p_o\}$, where t_R is the time elapsed between solute injection and the elution of the peak maximum, i.e. the retention time. The result is:

$$V_R = F_o t_R = \frac{V_M + K_L V_L}{j_3^2} \quad (8)$$

where j_3^2 is a compressibility correction factor, given by

$$j_3^2 = \frac{3[(p_i/p_o)^2 - 1]}{2[(p_i/p_o)^3 - 1]} \quad (9)$$

V_R is the *uncorrected retention volume*; since V_M , V_L and K_L are pressure independent, it is obvious that V_R depends on pressure. In order to suppress this dependence a *corrected retention volume*, V_R^o , is defined by:

$$V_R^o = j_3^2 V_R = j_3^2 F_o t_R = V_M + K_L V_L \quad (10)$$

For a non-sorbed solute with retention time t_M , from Eq. (10)

$$j_3^2 F_o t_M = V_M \quad (11)$$

t_M , known as *column hold-up time*, represents also the time that all solutes spend in the mobile phase during their travel between column inlet and outlet. It is one of the more important parameters of retention calculations.

Another important retention parameter is the *net retention volume*, V_N , obtained by subtracting Eq. (11) from Eq. (10):

$$V_N = V_R^o - V_M = j_3^2 F_o (t_R - t_M) = K_L V_L \quad (12)$$

By combining Eqs. (10) and (11) the following very important result is obtained:

$$t_R = t_M \left[1 + K_L \left(\frac{V_L}{V_M} \right) \right] = t_M (1 + k) \quad (13)$$

where $k = K_L(V_L/V_M) = K_L/\beta$ is known as *retention factor* and $\beta = V_M/V_L$ is the *column phase ratio*.

It is important to stress at this point that within the context of the basic retention theory V_R^o , V_N and V_M are pressure independent; as such they do not represent volumes reduced to any determined pressure. The same corresponds to K_L .

The carrier gas flow rate is most usually measured with a 50 ml or 100 ml soap bubble flowmeter, connected to the column outlet by means of a tube with negligible pressure drop. The flow rate measured at the flowmeter, $F(T_{fm})$, at the temperature T_{fm} and carrier partial pressure $p_{fm} - p_w \cong p_o - p_w$, where p_w represents the water saturation pressure at T_{fm} , must be corrected to the conditions prevailing at the column outlet, temperature T and pressure p_o :

$$F_o(T) = F(T_{fm}) \frac{T}{T_{fm}} \left(\frac{p_o - p_w}{p_o} \right) \quad (14)$$

Outlet pressure p_o is usually atmospheric pressure; T_{fm} can be room temperature, but it is more convenient to employ a water jacketed flowmeter connected to a water circulating thermostat.

The expression to calculate K_L , from Eq. (12), is:

$$K_L = j_3^2 F_o(T) (t_R - t_M) \left(\frac{\rho_L}{w_L} \right) \quad (15)$$

w_L is the mass of stationary phase and ρ_L is its density at the column temperature; j_3^2 and $F_o(T)$ are calculated by means of Eqs. (9) and (14), respectively.

K_L is closely related to the activity coefficient of the solute at infinite dilution in the molar fraction scale and using the symmetrical convention, $\gamma_1^{\infty*}$ [8]. The solute partial pressure over the solution within Henry's law region, p_1 , is given by:

$$p_1 = \gamma_1^{\infty*} x_1 p_1^o \quad (16)$$

where p_1^o is the solute saturation pressure and x_1 its molar fraction in the solution that, at infinite dilution, can be written:

$$x_1 = \frac{n_1^L}{n_1^L + n_3^L} \cong \frac{n_1^L}{n_3^L} = \frac{n_1^L v_3^o}{V_L} \quad (17)$$

where n_1^L and n_3^L are moles of solute and of stationary phase, respectively, and v_3^o is stationary phase molar volume. On the other side, for an ideal vapor phase,

$$p_1 V_M = n_1^M RT \quad (18)$$

where n_1^M represents moles of solute in the vapor phase. Using Eqs. (16)–(18) the following expression is obtained:

$$K_L = \frac{RT}{\gamma_1^{\infty*} p_1^o v_3^o} \quad (19)$$

Eq. (16) defines $\gamma_1^{\infty*}$ in terms of pressures; basic retention theory considers K_L as well as $\gamma_1^{\infty*}$ as pressure independent. Consequently $\gamma_1^{\infty*}$, intended to gauge deviations of the condensed phase from the ideal solution behavior, includes also deviations of the vapor phase from the ideal gas. A more rigorous approach that discriminates between these two effects is sketched in the following section.

2.2. Retention theory taking into account vapor phase non-idealities

Several authors have studied the means to relax the assumptions of the basic retention theory. This review shall be restricted to the work of Cruickshank et al. at the University of Bristol [9–11], who made use of Everett's treatment of the effects of gas imperfections on the gas–liquid partition coefficient [12].

Everett considered the state of equilibrium between a binary solution (components 1 and 3) in the presence of a gas (component 2) which is insoluble in the condensed phase, with component 1 distributing between both phases while 3 is very scarcely volatile. For pressures usual in GLC the volumetric behavior of the gas can be described with negligible error by means of the virial equation explicit in pressure and truncated to the second coefficient [13]:

$$v = \frac{RT}{p} + B \quad (20)$$

where v represents the molar volume of the gas and B is the second virial coefficient, dependent on temperature and composition. For a binary mixture with components at molar fractions y_1 and y_2 the expression is:

$$B = y_1^2 B_{11} + 2y_1 y_2 B_{12} + y_2^2 B_{22}$$

where B_{11} and B_{22} are the second virial coefficients for the components in their pure state and B_{12} characterizes interactions in their mixtures.

The equation deduced by Everett for the partition coefficient at infinite dilution, with Eq. (20) as the only assumption, is:

$$\ln K_L = \ln \frac{RT}{\gamma_1^\infty(T, 0) v_3^\infty p_1^\infty} - \frac{(B_{11} - v_1^\infty) p_1^\infty}{RT} + \frac{(2B_{12} - v_1^\infty) p}{RT} \quad (21)$$

v_1^∞ and v_3^∞ are the molar volumes of solute 1 and solvent 3, respectively, v_1^∞ is the solute partial molar volume at infinite dilution in 3, and $\gamma_1^\infty(T, 0)$ is the solute activity coefficient at infinite dilution and zero pressure. The difference between $\gamma_1^{\infty*}$ and $\gamma_1^\infty(T, 0)$ resides in that this last measures only deviations from the ideal solution behavior, while also gas imperfections are included in $\gamma_1^{\infty*}$. Since its first two terms are pressure independent, Eq. (21) can be written as:

$$\ln K_L = \ln K_L^\circ + \beta p \quad (22)$$

with K_L° representing the solute gas–liquid partition coefficient at infinite dilution and zero pressure and:

$$\beta = \frac{2B_{12} - v_1^\infty}{RT} \quad (23)$$

Note that even for an ideal gas mixture (i.e. $B_{12} = 0$) β differs from zero, making K_L pressure dependent.¹

According to Eq. (20), the effect of pressure drop on the carrier gas volumetric flow rate is now given by Eq. (24):

$$\frac{Fp}{1 + bp} = \frac{F_o p_o}{1 + b p_o} \quad (24)$$

with $b = B_{22}/RT$. At pressures below 50 atm the viscosity of real gases is adequately described with the Chapman–Enskog equation [14],

$$\eta = \eta_o(1 + ap) \quad (25)$$

with $a = 0.175 B_{22}/RT$.

When Eqs. (22), (24) and (25) are introduced in Eq. (2), an extremely complex expression is obtained, containing two integrals that do not admit analytical evaluation. Cruickshank et al. carried out their evaluation by an expansion in series, obtaining expressions that, although extremely unwieldy, permit numerical calculations on experimental data. Their conclusion was that in packed columns, at pressures lower than 20 atm and pressure drops below 2 atm, the effects of carrier gas imperfections are not detectable experimentally. Under the assumption of an ideal carrier gas and a solute that interacts non-ideally with it (i.e. $B_{12} \neq 0$) integration is feasible and leads to the following result:

$$\ln V_N = \ln V_N^\circ + \beta p_o J_3^4 \quad (26)$$

where V_N is defined as in Eq. (12), $V_N^\circ = K_L^\circ V_L$ is the value of V_N measured under the conditions $p_i = p_o = 0$, and:

$$J_3^4 = \frac{3[(p_i/p_o)^4 - 1]}{4[(p_i/p_o)^3 - 1]} \quad (27)$$

Since K_L° is free from gas imperfections effects, its determination is the ultimate objective in meticulous thermodynamic measurements. The recommended procedure is to plot $\ln V_N$, measured at several pressures and calculated according to Eq. (12), against $p_o J_3^4$; $\ln V_N^\circ$ is taken from the intercept and β from the slope. Methods to estimate B_{12} from β have been proposed by several authors and a detailed review can be read in Laub and Pecsok's book [2]; all of them demand the approximation $v_1^\infty \cong v_1^\circ$. When values of V_N at several pressures are not available an estimation of gas imperfection effects can be made by using B_{12} values predicted by one of several proposed methods [13] together with the mentioned approximation. Thus obtained results are of questionable validity and not always the information they demand is available; however they give an estimation of the effects and, in case the author considers them as important in relation with other sources of error, measurements at several pressures are advisable.

Corrections are in general low (0.2–5%) when hydrogen, helium or nitrogen are used as carrier gases at usual

¹ Unfortunately, β is also used to represent the column phase ratio in the chromatographic literature.

chromatographic pressures. The solubility of the carrier gas at high pressures can introduce an additional error.

3. Retention by mixed mechanisms

The assumption that gas–liquid partition is the only mechanism responsible for solute retention is implicit in the models described in the former points; however, as has been demonstrated in several occasions, other retention mechanisms can take place simultaneously with partition. Although several processes have been proposed, rather artificially in some instances, realistic and practical considerations indicate that only the following need be taken into consideration:

- (a) Strong interactions between some solutes and active sites on the solid support (silanol groups, metallic impurities, etc.) result in solute adsorption on the solid-stationary phase interface (SLI) or on uncoated portions of the solid (GSI). These distribution processes, specially important for polar solutes, are characterized by highly curved isotherms whose linear regions are not even reached at the lower solute concentrations compatible with high sensitivity detectors. In other words, if present they usually result in asymmetrical peaks.
- (b) Mixtures displaying strong positive deviations from the ideal solution behavior result in solute adsorption at the gas–liquid interface (GLI); therefore the occurrence of this mechanism has to be suspected for systems displaying large infinite dilution activity coefficients. The linear ranges of the adsorption isotherms are larger than those for adsorption on the GSI or on the SLI, but non-linearity starts at solute gas phase concentrations at which partition still behaves linearly. Adsorption on the GLI can be more insidious than adsorption on the solid: while this last is generally revealed by asymmetrical peaks, the former can pass unnoticed, and the literature abounds in papers reporting very high activity coefficients with no test for adsorption carried out; K_L can in these cases be affected by important systematic error.

Retention in the presence of these concurrent distribution processes has been described by equations of the type [15,16]:

$$V_N = K_L V_L + K'_A A_L + K'_I A_I + K'_S A_S \quad (28)$$

where A_L , A_I and A_S represent the surface areas of the GLI, SLI and GSI, respectively, and K'_A , K'_I and K'_S are the slopes of the adsorption isotherms on the three mentioned surfaces; primes denote finite concentrations, i.e. a non linear region of the isotherm. As mentioned, basic chromatographic theory tells that if infinite dilution is not attained by any of the distribution processes, resulting peaks shall be asymmetric, their maxima displaying sample size-dependent retention times. Several methods to measure K_L in the presence of asymmetry have been discussed by

Zhang et al. [17], who concluded that accurate measurement of partition coefficients demand that adsorption effects be minimized.

Symmetric peaks are therefore a prerequisite for the measurement of any thermodynamic quantity. Classical diatomaceous supports pose in this sense serious difficulties for the study of even moderately polar solutes, specially with non polar stationary phases. Considerable improvement is attained by using silane-treated supports, specially when used with moderate to high polarity stationary phases. However highly polar solutes, as alcohols and amines, elute as asymmetric peaks from columns packed with low polarity stationary phases coated on silane-treated supports.

High purity fused silica capillary columns are promissory tools in the study of different families of solutes, even with low polarity phases; Zhang et al. [17] obtained sample size independent retention times for a numerous and diverse group of solutes in silica capillary columns coated with hexadecane. More recently, Castells et al. [18] obtained sample size independent retention times for alcohols in columns packed with squalane coated on Chromosorb W deactivated by an ultrathin film of Carbowax 20M, prepared according with the procedure of Aue et al. [19]. Deactivation by Aue's method, however, seems to be specific for alcohols; other functionalized polymers may be efficient deactivators for other families of highly polar solutes, this being a subject worthy of investigation.

Due to its high incidence on the accuracy of the results, it is necessary to make quite sure that measurements are being performed under infinite dilution conditions. Visual observation and measurement of peak symmetry is a first test. Cruickshank and Everett [20] suggested measurement of the skew factor η , defined as the ratio of the absolute value of the rear to front tangent slopes; peaks with η larger than 1.2 or smaller than 0.8 should not be used. A better indication is obtained by injecting samples of different size and then plotting the retention time of the peak maximum against peak area [17,18]; this method is free of subjectivities, is more sensitive, and gives direct information about the range of sample size within which Henry's law is obeyed.

It must be stressed that sample size independent retention times means that all the retention mechanisms are operating under infinite dilution conditions, but not the absence of adsorption contributions to retention. Peak symmetry usually means that solid support effects are absent; under these conditions Eq. (28) can be written as:

$$V_N = K_L V_L + K_A A_L \quad (29)$$

In order to detect adsorption contributions V_N is measured in several columns containing different weight fraction of stationary phase; these usually range between 0.02 and 0.15 for white diatomite supports and between 0.02 and 0.25 for the pink ones. Then V_N/V_L is plotted against $1/V_L$ and the

resulting plot is analyzed in terms of Eq. (29). Two behaviors are possible:

- The plot is an horizontal line when adsorption does not contribute to retention; in this case the height of the line is $V_N/V_L = K_L$.
- A parabola convex to the abscissa axis is obtained when adsorption effects are present; in this case extrapolation to $1/V_L = 0$ gives K_L .

On the condition that peaks are symmetrical, K_L can be obtained in case (b) independently that adsorption occurs by one or more mechanisms. It is quite obvious that partition coefficients obtained through extrapolations as those mentioned under (b) are considerably less accurate than those measured in systems where no type of adsorption contribution is present.

4. Column hold-up determination

The retention time of a non sorbed solute or column hold-up time, t_M , is a fundamental parameter for the determination of any thermodynamic function; an incorrectly measured t_M is source of a systematic error whose magnitude must be evaluated. The retention time of the air peak has been taken as t_M in the work with katharometers; the use of neon has also been suggested since it has shown smaller retention times in most chromatographic systems [21]. The retention time of the methane peak has been the most usual choice in the work with flame ionization detectors (FID); this gave rise to many discussions and alternative proposals.

Since methane shows some retention (specially in non polar stationary phases), alternative methods to estimate t_M on different basis were developed. They make use of Eq. (13), that can be written as:

$$t_R(n) = t_M[1 + k(n)] \quad (30)$$

where $t_R(n)$ represents the retention time of a normal alkane with n carbon atoms and $k(n)$ is its retention factor. A linear relationship between $\ln k(n)$ and n was initially assumed, this leading to equations like:

$$\ln [t_R(n) - a] = b + cn \quad (31)$$

Several methods have been used to fit the retention times of a group of n -alkanes (measured on the same chromatogram) to Eq. (31); they were reviewed by Smith et al. [21,22]. The value of a that produces the best fit is taken as t_M in these methods; thus calculated t_M have been called mathematical hold-up times.

The linear relationship has been questioned by many authors. García-Domínguez and co-workers [23,24], for instance, detected statistically significant deviations from linearity for the retention times of normal alkanes on six packed and three capillary columns. They observed that mass-spectroscopically measured retention times of Ne, Ar, N₂, O₂ and methane are very close, and that not always

Table 1

Ratios $t_R(C_1)/t_M$ calculated by means of Eq. (35) for two packed and one capillary column at several values of $K_L(C_1)$

$K_L(C_1)$	$\beta = 10$	$\beta = 40$	$\beta = 150$
0.1	1.010	1.003	1.001
0.5	1.050	1.013	1.003
1.0	1.100	1.025	1.007
1.5	1.150	1.038	1.010
2.0	1.200	1.050	1.013
2.5	1.250	1.063	1.017

Ne is the least retained solute; furthermore, Ne elutes after methane from some columns. The authors tested 25 empirical equations with three to five parameters, and selected the following two on the basis of quality of the fit and differences between predicted t_M and retention time of Ne:

$$t_R(n) = A + \exp(B + Cn + Dn^2) \quad (32)$$

$$t_R(n) = A + \exp(B + Cn^D) \quad (33)$$

t_M is estimated as the retention time of an n -alkane with $n = 0$ (i.e. $t_M = A + \exp B$); the results obtained by means of both equations are coincident or very close.

An equation based on a retention model for n -alkanes deduced from basic concepts of statistical thermodynamics was more recently proposed by Gonzalez [25]:

$$t_R(n) = t_M + \exp[A + B(n - 2) + \ln(1 - Cn^2)] \quad (34)$$

Multiparametric non linear regression of experimental retention times of n -alkanes with $n \geq 5$ is performed by means of commercial software that applies Marquardt algorithm [26]; estimations made with Eq. (34) are slightly smaller than those obtained with Eq. (32) or Eq. (33).

On account of the widespread use of flame ionization detection with methane as hold-up marker, it is interesting to estimate what the consequences of this practice can be. In the first place we must consider that, according to Eq. (30), t_M and methane retention time, $t_R(C_1)$, are related by the expression:

$$\frac{t_R(C_1)}{t_M} = \frac{\beta + K_L(C_1)}{\beta} \quad (35)$$

where $K_L(C_1)$ is methane gas-liquid partition coefficient. The ratios $t_R(C_1)/t_M$ calculated by means of Eq. (35) for different values of β and $K_L(C_1)$ have been gathered in Table 1. The values of $K_L(C_1)$ cover the range of results reported by several authors in paraffinic and non polar silicone solvents at ambient and higher temperatures. $\beta = 10$ is the phase ratio grossly calculated [27] for a packed column whose stationary phase weight fraction is 0.20, with Chromosorb W as solid support, while $\beta = 40$ is the result obtained by the same calculation for a stationary phase weight fraction of 0.05; $\beta = 150$ is the nominal phase ratio for a capillary column, 0.2 mm inner diameter and 0.33 μm film thickness. The results demonstrate that $t_R(C_1)$ and t_M can be very different, specially for packed columns with high stationary

Table 2
Retention factors calculated by using different hold-up times and relative error in K_L resulting from the use of methane as t_M marker

n	$t_R(n)/s$	k^{*a}	k^b	$-\varepsilon^c$
1	158.6	0	0.092	–
5	321.0	1.024	1.211	0.076
6	465.3	1.934	2.205	0.042
7	725.0	3.571	3.993	0.023
8	1191.9	6.515	7.209	0.013
9	2025.7	11.772	12.951	0.007

Consult the text for details on the experimental t_R of n -alkanes.

^a $k^* = [t_R(n) - t_R(C_1)]/t_R(C_1)$.

^b $k = [t_R(n) - (t_M)]/t_M$, with $t_M = 145.2$ s [27].

^c Calculated with Eq. (37).

phase weight fraction. In order to obtain a more physical insight it can be illustrative to mention that statically measured $K_L(C_1)$ in n -hexadecane near room temperature reported by several authors are in the range 0.45–0.51 [28], and that calculations carried out by Gonzalez [27] on retention data of n -alkanes in poly(dimethylsiloxane) capillary and packed columns indicate that $K_L(C_1)$ drops from 2.6 to below 1.0 in the range 40–120 °C.

According to Eq. (15) the relative error, ε , of the partition coefficient K_L^* calculated by assuming $t_M = t_R(C_1)$ for a solute whose retention time is t_R is given by the expression:

$$\varepsilon = \frac{K_L^* - K_L}{K_L} = \frac{t_M - t_R(C_1)}{t_R - t_M} \quad (36)$$

that on using Eqs. (13) and (35) can be written

$$\varepsilon = \frac{t_M - t_M[1 + k(C_1)]}{kt_M} = -\frac{k(C_1)}{k} = -\frac{K_L(C_1)}{K_L} \quad (37)$$

where k is the solute retention factor. Results calculated with the retention times measured at 120 °C on a packed column (stationary phase weight fraction 0.194, PS-255 on Chromosorb W AW DMCS, 4 m × 2.2 mm) [24] can be read in Table 2. Retention factors listed in the third column were calculated by assuming $t_M = t_R(C_1)$ and those in fourth column by using $t_M = 145.2$ s, as calculated in [27]. Relative errors are listed in the fifth column.

Relative errors drop to about one half if the value of t_M estimated by García-Domínguez et al. [24] (151.1 s) is used in the calculations and to about one third if Ne retention time (152.7 s) is used as t_M . With independence of the criterion applied to estimate t_M these results indicate that the systematic errors introduced by using methane as hold-up time marker are larger than those resulting from neglecting vapor phase imperfections. Although there is at the present no widely accepted criterion to determine t_M and the subject demands more investigation, Gonzalez's proposal, based on theoretical retention model, seems to be the most appropriate choice. It must be pointed out that Eq. (34) assumes that partition is the only retention mechanism, and a modification to deal with systems in which adsorption contributions are not negligible has been described in a later paper [29].

5. Determination of the stationary phase volume, V_L

The liquid density must be measured at several temperatures covering the experimental range; the results are then fitted to an adequate equation. Once the density is known as a function of temperature the problem is reduced to the determination of the weight w_L of stationary phase. Laub et al. [30] demonstrated that this is the largest source of systematic error in K_L measurement by means of packed columns.

The weight fraction of stationary phase in the packing could in principle be calculated from the carefully measured weights of thoroughly dried support and stationary phase; however a not negligible fraction of this last can be lost on the walls of the vessel used for the evaporation of the solvent employed in the coating operation. In order to minimize this error Laub et al. [30] determined the mass fraction of stationary phase from the mass loss on ashing (700–1000 °C) in porcelain crucibles of tared amounts of packing; a correction for bare support losses is determined by the same method. Percentage standard deviations calculated from replicate measurements carried out on packings containing about 10% (w/w) squalane or dinonyl phthalate on Chromosorb G AW DMCS ranged between 0.3 and 1.0%. A different approach was applied by Wicarova et al. [31]: they extracted their packings in a Soxhlet apparatus, evaporated the solvent and weighed the residue, a procedure said to be accurate to about half a milligram.

Finally, the weight of packing in the column must be determined; Laub et al. [30] removed the injection-end glass wool plug and displaced the column contents into a tared filtering flask with a coarse glass frit in its side arm.

6. Packed or capillary columns?

Several reasons, besides the already mentioned difficulty in immobilizing some liquids on the capillary walls, determine the scarce use of capillary columns in the measurement of K_L .

One of the reasons is that retention volume has been the variable currently used by chromatographers. Some of the parameters required to transform retention times into retention volumes and then into partition coefficients are of difficult accurate measurement in the work with capillary columns; this is the case of flow rate and weight of stationary phase. However, in spite of tradition, it must be recognized that time, and not volume, is the natural, directly measured retention variable. Partition coefficients and retention times are related by:

$$K_L = \beta \left(\frac{t_R}{t_M} - 1 \right) \quad (38)$$

This equation restricts the problem to that of measuring t_R , t_M and β . Due to a series of reasons capillary columns are notoriously superior to packed ones for the measurement of these three quantities:

- (a) A larger number of *n*-alkanes can be accommodated in a capillary chromatogram, thus improving the measurement of t_M .
- (b) Since peaks eluting from capillary columns are narrower, their maxima are better defined.
- (c) Peaks of perfect symmetry are not possible due to extra column effects; as a consequence, the retention time of the peak maximum does not coincide with the residence time of peak center of gravity (which defines peak position in Eq. (2)). The difference between these two times is proportional to the skew ratio and to the peak width at half height; since peak width increases with retention time, the difference is not constant for all the alkanes. Because of their wider peaks, these effects are more important in packed columns and can introduce large errors in the determination of t_M .
- (d) The phase ratio of packed columns is calculated by means of the equation:

$$\beta(T) = j_3^2 F_o(T) \rho_L(T) \frac{t_M}{w_L} \quad (39)$$

that involves highly uncertain parameters, such as t_M and w_L . Phase ratio of capillary columns has been grossly calculated from the tube internal diameter d_c and film thickness d_f as $\beta \cong d_c/4d_f$. For columns prepared by the static method β can be calculated at any temperature, assuming a constant thermal expansion coefficient for the silica wall α_{SiO} , by means of the expression [32]:

$$\beta(T) = \frac{\rho_L(T)}{C_o} \exp[\alpha_{SiO}(T - T_o)] - 1 \quad (40)$$

C_o is the concentration of the stationary phase solution employed for filling the capillary at the temperature T_o . β can be calculated with four significant digits if an adequate amount of coating solution is prepared.

The justified belief in that construction of capillary columns is a very difficult task, with numerous secrets and of uncertain result, in contrast with the apparent easiness of constructing packed columns, has probably been the principal obstacle to the diffusion of the employment of capillary columns for thermodynamic studies. However, although packed columns are easily constructed, the accurate measurement of their characteristic parameters (t_M , β) is not simple. An additional and not negligible advantage of fused silica capillary columns is a more inert solid surface.

On the other side important progresses have been done in the methods used for filling capillary tubes. The static method, that in previous versions demanded days to vacuum evaporate the solvent, has been modified and a new column can be prepared in hours. A high temperature evaporation method was developed [32], using a special oven for this purpose.

It can be envisaged that the possibility of an accurate measurement of β and t_M shall promote the employment of capillary columns for the measurement of K_L and of other thermodynamic functions.

7. IUPAC recommendations on chromatographic parameters

The two latest publications of IUPAC on chromatographic nomenclature and symbols [33,34] cover aspects directly related to the subject of the present review.

- (a) The name *distribution constant* and the symbol K_C is recommended for what generations of chromatographers have called *partition coefficient* and symbolized with K_L . The gas–liquid partition coefficient is a special case, not specifically mentioned in IUPAC publication. Since there is no possible conceptual confusion about its meaning, the traditional name and symbol were retained in the present paper.
- (b) The use of the *specific retention volume at 0 °C*, defined as:

$$V_g = 273.15 \frac{V_N}{w_L T} \quad (41)$$

is discouraged by IUPAC.

- (c) The term *dead time*, traditionally use as synonymous of *hold-up time*, has also been discouraged by IUPAC.
- (d) For the determination of the hold-up time IUPAC recommends the non-linear fitting of the retention times of a *minimum of five n-alkanes including methane* to Eq. (33). Eq. (34), deduced from an elementary statistical mechanics model, appeared in a paper [25] published almost simultaneously with the latest IUPAC recommendation. Because of its theoretical foundations we understand that Eq. (34) surpasses Eq. (33), proposed only on empirical basis

8. Conclusions

GLC is a powerful and attractive tool for the measurement of K_L ; it is instrumentally simple, requires very small quantities of the test substances in not too high degrees of purity, the temperature is easily modified and a large quantity of data can be collected in relatively short times. However, its apparent simplicity can be misleading and the information it brings can be erroneous if some of its complex aspects are not correctly perceived and taken into consideration. The number of experimental parameters to be controlled is not small, not always the commercial instruments are apt for this task and the sources of systematic error listed in this review must be under control.

Symmetrical peaks constitute the first requisite to be fulfilled; results calculated from asymmetrical peaks are valueless; the authors should demonstrate with experimental evidence that their measurements were carried out at infinite dilution. The second requisite is to make quite sure that partition is the only retention mechanism operating in his chromatographic system. This can be checked by comparing results obtained on two columns with considerably different stationary phase weight fraction; if adsorption effects

are detected, additional columns covering a range of weight fractions should be used to correct for them. Column hold-up time must be correctly measured. Replicates are indispensable, since K_L data are of little value if their error limits are not specified. Corrections for gas phase imperfections are pertinent only in those cases in which the mentioned systematic errors are absent or fully minimized.

Finally, it is to be expected that the characteristics of capillary columns pointed out in the present review shall serve to persuade about their advantages in the measurement of partition coefficients.

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