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THE CAPACITY OF LABORATORY-SCALE PREPARATIVE CHROMATOGRAPHY COLUMNS

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SUMMARY

It was found that a relationship exists between the capacity of gas chromatographic columns and the different experimental parameters for the linear part of the sorption isotherm.

Preparative gas chromatography is finding ever increasing applications not only in purely laboratory preparative work but also in the semi-industrial production of pure substances. The problem of the capacity of preparative units is of decisive importance here. It is expedient to characterise the capacity as the amount of the mixture separated per unit time at a given degree of separation (or the degree of purity of the substances obtained). The latter is usually determined by the resolution value R

$$R = \frac{2(V_2 - V_1)}{\Delta S_1 + \Delta S_2} \tag{1}$$

where V_1 and V_2 are the retention volumes of the first and second components, respectively; ΔS_1 and ΔS_2 are widths of the peaks corresponding to these components.

An expression for the capacity of greatly overloaded columns under the conditions of stepwise chromatography at $R = 1$ has been derived by ALEKSEEVA et al.[1]. To correlate the capacity and the experimental parameters, use can be made of the theory of VAN DEEMTER et al.[2]. According to this theory, when introducing a vapour-like sample of volume A, the band width is

$$\Delta S = A + v \sqrt{2\pi n_0} \tag{2}$$

and the retention volume is

$$V = n_0 v + \tfrac{1}{2} A \tag{3}$$

where n_0 is the number of theoretical plates in the absence of overloading; v the effective volume of a theoretical plate. These equations hold provided that the sorption isotherm is linear and the sample is introduced by the "plug injection" method. If

the value for A is represented as the product $V_s K_m$, where V_s is a volume of a sample undiluted by a carrier gas and K_m is a dilution factor[3], then by substituting (2) and (3) into eqn. 1, the expression for the peak resolution value under overloading conditions will be

$$R = \frac{2\,n_0\,K_s}{\dfrac{2\,V_s K_m}{v_1 + v_2} + \sqrt{2\,\pi\,n_0}} \tag{4}$$

where $K_s = \dfrac{v_2 - v_1}{v_2 + v_1}$ is a selectivity factor.

Making use of the apparent relation $v_1 + v_2 = \dfrac{SL\,(\Gamma_1 + \Gamma_2)}{n_0}$ where S is the cross-section, L is the column length, and Γ is Henry's general coefficient, we obtain

$$R = \frac{2\,K_s}{\dfrac{2\,V_s K_m}{SL\,(\Gamma_1 + \Gamma_2)} + \sqrt{\dfrac{2\pi H_0}{L}}} \tag{4a}$$

where H_0 is height of an effective theoretical plate (HETP) in the absence of overloading. One can see from this equation that resolution under the overloading conditions is proportional to K_s. To a lesser degree, it depends on effective-diffusion washing-out characterised by H_0. The first term in the denominator is defined by the volume of the dose introduced, $K_m V_s$, and by the column volume, SL, and its sorption holding capacity, Γ.

From eqn. 4a, the volume of the mixture, V_s, separated at a given value R can be expressed as

$$V_s = \frac{SL\,(\Gamma_1 + \Gamma_2)}{K_m R} \left(K_s - \tfrac{1}{2} R\,\sqrt{\dfrac{2\pi H_0}{L}}\right) \tag{5}$$

By definition, the capacity of the unit is

$$P = \frac{V_s}{\tau} \tag{6}$$

where τ is the separation cycle time calculated from the moment of introduction up to complete elution of the second peak

$$\tau = \frac{n_0 V_2 + K_m V_s + \tfrac{1}{2} V_2 \sqrt{2\pi\,n_0}}{W} \tag{7}$$

where W is the gas flow-rate.

Substituting (5) and (7) into formula 6 and making some simplifications, we obtain

$$P = W\,\frac{\dfrac{\alpha + 1}{\alpha}}{R + \tfrac{1}{2}\dfrac{\alpha - 1}{\alpha}} \left(K_s - \tfrac{1}{2} R\,\sqrt{\dfrac{2\pi H_0}{L}}\right) \tag{8}$$

where $\alpha = \dfrac{V_2}{V_1}$ is a separation factor.

Formula 8 holds for the case when the mixture is supplied to the chromatographic column as a squared pulse with concentration C_0 corresponding to a linear region of the sorption isotherm. But in most preparative chromatographs, the mixture rapidly evaporates in the overheated evaporator and is supplied to the column at high concentration. Therefore, a check on the validity of eqn. 2 for these conditions was made. A column, 14 mm in diameter and 3 m in length, was filled with INZ-600 as column packing and 20% of dinonyl phthalate. Increasing volumes of liquid mixtures containing diethyl ether, 2,2-dimethyl butane, hexane, benzene, pentane and dichloroethane were introduced through an evaporator into a steady carrier gas flow. A metallic cylinder with a spiral packing heated externally serves as an evaporator. The evaporator temperature was higher by 30 to 40° than the average boiling point of the mixture introduced.
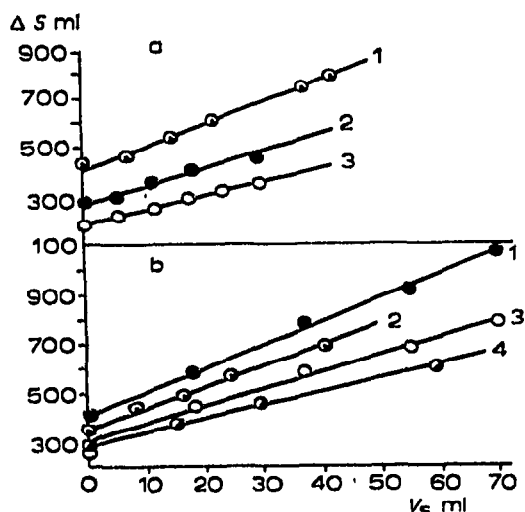

Fig. 1. Peak width dependence (in gas ml) on sample volume. (a) Column temperature 70°. 1 = cyclohexane; 2 = hexane; 3 = 2,2-dimethyl butane. (b) Column temperature 95°: 1 = dichloroethane; 2 = benzene; 3 = carbon tetrachloride; 4 = cyclohexane.

In all the cases, the proportionality between the peak width and sample volume was satisfactory (Fig. 1). The slope of the straight line, $i.e.$ the K_m factor did not change as the gas velocity increased from 50 up to 500 ml/min and the column length increased from 2 up to 10 m. However, K_m was dependent on the distribution coefficient, increasing with its growth. In fact, K_m decreased with increasing column temperature and became practically constant at temperatures close to the boiling point of the substance. K_m is different for various substances, increasing with the retention volume. At temperatures close to the boiling point of the substance, this difference is small. Inconstancy in K_m, probably due to non-linearity in the sorption isotherm, leads one to regard it as a semi-empirical factor. Furthermore, it was found experimentally that the intercepts cut off by the straight lines on Fig. 1 are practically equal to the peak width at the introduction of a dose of several microlitres in volume when the column is not as yet overloaded. As a result of this, the numerical factor in eqn. 8 is equal to 4, rather than to $\sqrt{2\pi}$.

The deviations from eqn. 2 discussed, particularly the dependence of K_m on the nature of the substance, hinder the use of formula 8 in quantitative or even semi-quantitative calculations of the capacity. It was, however, found by us that the ratio

TABLE I

THE DEVIATIONS OF THE CHROMATOGRAPHIC PEAK SHAPE FROM THE GAUSSIAN CURVE

Experimental conditions				Sample volume (ml)	Asymmetry factor	a_2/a_1	% deviation	a_3/a_1	% deviation
Substance	Column diameter (mm)	Column length (m)	Temperature (°C)						
Cyclohexane	30	1.9	77	1.0	0.75	1.37	3.5	1.86	7.0
				3.0	0.61	1.37	3.5	1.81	9.5
				5.0	0.48	1.33	6.0	1.73	13.5
n-Pentane	30	3.5	20	0.6	0.92	1 36	4.0	1.89	5.5
				1.0	0.66	1.38	3.0	1.89	5.5
				2.0	0.61	1.35	5.0	1.82	9 0
				10.0	0 34	1.35	5.0	1 77	11.5
Benzene	15	1.9	95	4 μl	0.8	1.42	0	2.0	0
				0.2	0.36	1.36	4.0	1.77	11.5
Heptane	15	1.9	95	4 μl	0.6	1.40	1.5	2.0	0
				0.4	0.38	1.34	5 5	1.79	10.5

of K_m values obtained on preparative and analytical columns is practically the same for various substances. Having determined this ratio experimentally, one can then calculate K_m for a preparative column, based on the value determined for an analytical column.

Also of interest is a relationship between R and the purity of the fraction. The literature contains the methods for calculating the fraction purity for peaks described by Gaussian equations[4-6]. Under overloading conditions, the shape of a peak deviates from this equation. From the Gaussian equation of the curve, it follows that its width at a distance $e^{-0.5}$ (0.607) of the whole height (a_2) is to the width at a distance e^{-1} (0.367) of the whole height (a_1) as 1.42:1. Accordingly, the width at a distance e^{-2} (0.134) of the whole height (a_3) is to a_1 as 2:1.

We have calculated the peaks of various hydrocarbons obtained on columns with dinonyl phthalate. Table I lists the results of some measurements, viz. the a_2/a_1 and a_3/a_1 ratios, their deviations from the theoretical values as a percentage, and the asymmetry factors equal to the ratio of the front and the back peak half-widths (measured at the half-height). For a not too large overloading (the sample volume is of the order of 0.5 ml for a column of 15 mm in diameter; for a 30 mm column, it is of the order of 2–3 ml), the deviation from the Gaussian curve is not too great, viz. 5–6% for the a_2/a_1 ratio and about 10% for the a_3/a_1 value. Under these conditions, satisfactory agreement can be expected between the calculated and experimentally determined purity of a fraction. With a large R value, the peak "tail" has a decisive influence on the purity of the fraction and the assumption of the Gaussian character of the distribution seems to be poorly founded. If traps are switched midway between the maxima of the peaks, the impurity of fractions with a mixture of equimolecular composition is determined by the formula (see ref. 6)

$$\eta = \frac{1}{2.82 \sqrt{\pi} R} e^{-2R^2} \tag{9}$$

and varies directly with the proportion of the components in the mixture.

To check the accuracy of the calculation of fraction purity, a model mixture of heptane and benzene was separated on a column 15 mm in diameter and 1.9 m in length packed with dinonyl phthalate on a solid carrier INZ-600; the fractions selected were analysed using the Pan-Chromatograph. The traps were switched at a point equidistant from maxima of both the peaks. The experimental data and results of calculations by means of formula 9 are presented in Table II, which also gives the results of the calculation with a correction for the symmetry of the peaks. Although the calculation of fraction purity is only semiquantitative, usually a certain range or an upper level is preset rather than the determination of the exact impurity content; such a calculation is of use in most cases. As could be expected, the greatest error is related to the peak asymmetry.

TABLE II

EXPERIMENTAL AND CALCULATED DEGREES OF FRACTION PURITY (%)
Mixture of heptane and benzene.

Component proportion	Sample volume (ml)										
	0.5				0.3				0.1		
	R	η exp.	η theor. 1	η theor. 2	R	η exp.	η theor. 1	η theor. 2	R	η exp.	η theor. 1
50:50	0.9	0.5	4	1.0	1.25	0.1	0.8	0.07	1.7	0.04	0.05
		2.0	4	—		—	—	—		—	—
70:30	1.0	1.0	1.0	—	1.35	0.1	0.15	—	1.8	0.03	0.01
		1.5	5.0	—		0.9	0.6				
80:20	1.05	0.8	0.6		1.4	0.15	0.07				

Note: 1. The upper line: purity of the first fraction; the lower: purity of the second fraction.
2. $\eta_{t\ldots 1}$ is the impurity calculated neglecting peak asymmetry;
$\eta_{t\ldots 2}$ is that taking account of peak asymmetry.

THE INFLUENCE OF THE SEPARATION CONDITIONS ON THE CAPACITY

Eqn. 8 can be used for the qualitative estimation of the effect of the experimental parameters on the capacity. The capacity was experimentally determined as follows: a dose which provides a prescribed R value was determined from the plot of R versus the volume of mixture to be separated. The capacity was further calculated by dividing the dose value by the separation time.

First of all, let us consider the influence of the column length. The second term in parentheses of eqn. 8 decreases to zero with increasing column length, while the capacity approaches the asymptotic limit P_{as}. Given the ratio P/P_{as}, the limit above which it is not advantageous to increase the column length can be determined. If it is assumed that the ratio equals 0.9, then

$$L_{\max} = 50\pi \frac{R^2}{K_s^2} H_0 \tag{10}$$

With a decrease in the selectivity factor and an increase in R, the maximum

length of the column increases. Thus, the more difficult the mixture to be separated and the higher the requirements of product purity, the longer the column that must be used.

With a simultaneous increase in gas velocity and column length, the capacity should increase proportionally with length. With great pressure drop, however, it also will tend to an asymptotic limit.

The experiments on the influence of column length on the capacity were performed at room temperature on the column 15 mm in diameter, packed with INZ-600 as solid carrier and dinonyl phthalate. The model mixture consisted of isopentane and n-pentane with nitrogen as carrier gas. The dependence of capacity on column length at constant average gas velocity is given in Fig. 2. As seen from Fig. 2, with increasing column length, the capacity increases up to a definite limit only. It is of interest to note that with increasing diameter, H_0 increases as a rule, moderating the capacity increase. However, if the column length is increased simultaneously with diameter so that the ratio is constant, then the capacity can be increased in proportion with the column cross-section. In this case, the simultaneous increase in column length and diameter may be advantageous.

With an increase in the flow rate of the carrier gas, the capacity should pass through a maximum according to eqn. 8 provided that $H_0 = CW$. The position of the maximum will be determined by the relationship

$$w_{max} = \frac{8}{9\pi} \frac{K_s^2 L}{R^2 C} \tag{11}$$

w is the gas flow rate per unit column cross-section.

With increasing R and decreasing K_s, the maximum rapidly shifts in the direction of low flow rates. This is confirmed by the experimental data obtained on the column 30 mm in diameter and 3 m in length which are given in Fig. 3.

It follows from formula 8 that the capacity is nearly proportional to $K_s = \alpha - 1/\alpha + 1$, as the expression before the parentheses containing α only slightly affects this dependence. To check the dependence of P on K_s, binary mixtures of hydrocarbons and chlorohydrocarbons with various K_s values were separated on a column with dinonyl phthalate. As seen from Fig. 4, the capacity is proportional to K_s, though dispersion of the points is rather wide. The use of high-selective phases is one of the most promising techniques for increasing the capacity of gas chromatographic columns. Using such phases for separating substances with close boiling points, one may obtain a capacity similar to that of a rectifying column. For instance, the capacity of the laboratory rectifying column with a spiral packing is 2.1 ml/h cm² for a mixture of benzene and carbon tetrachloride with the composition varying from 24 to 92 % of benzene, while the capacity of a gas chromatographic column of 6.7 m in length with dinonyl phthalate is 1.3 ml/h cm². For the benzene–cyclohexane mixture, where the difference in boiling temperatures of the components is 0.5°, the capacity is 2.5 to 3.0 ml/h cm² on a chromatographic column of 1.8 m in length with dinonyl phthalate, while in the stationary phase bis(propionitrile)-ethylene glycol, the capacity calculated from the experimental data by Bayer is 12 g/h cm². When purifying reagents to 99.90–99.995 % purity, the capacity of chromatography usually is 2 to 3 ml/h cm², and sometimes up to 6 ml/h cm² according to our data. These examples show that it is possible to use eqn. 8 for qualitative estimation of the effect of experimental param-
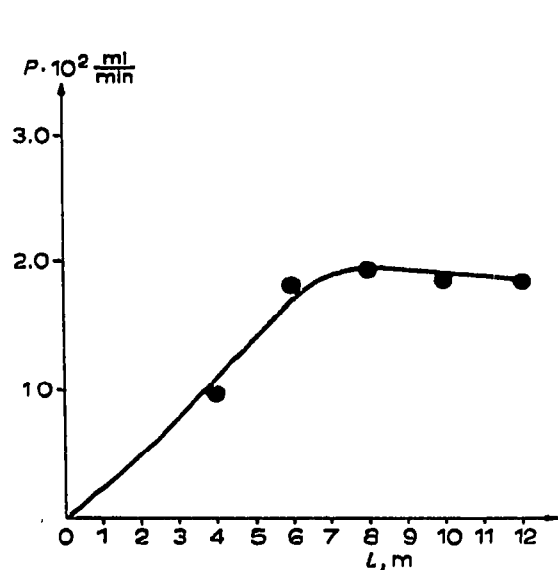
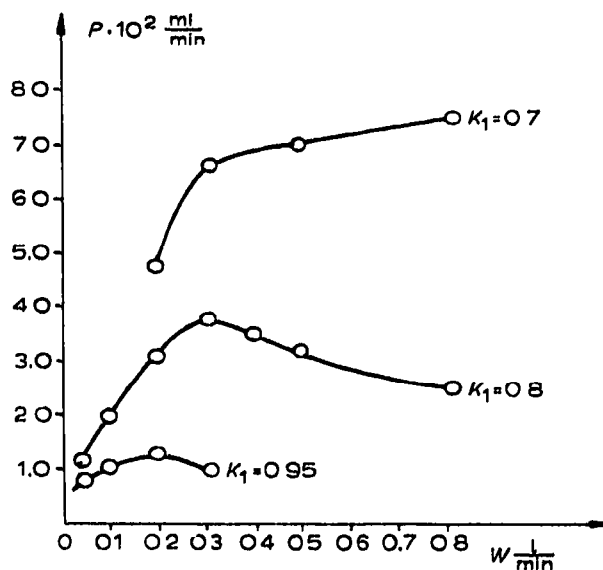Fig. 2. Capacity dependence on column length. Mixture of isopentane and n-pentane.

Fig. 3. Changes in capacity with increasing flow rate of carrier gas at various values. Mixture of isopentane and n-pentane.
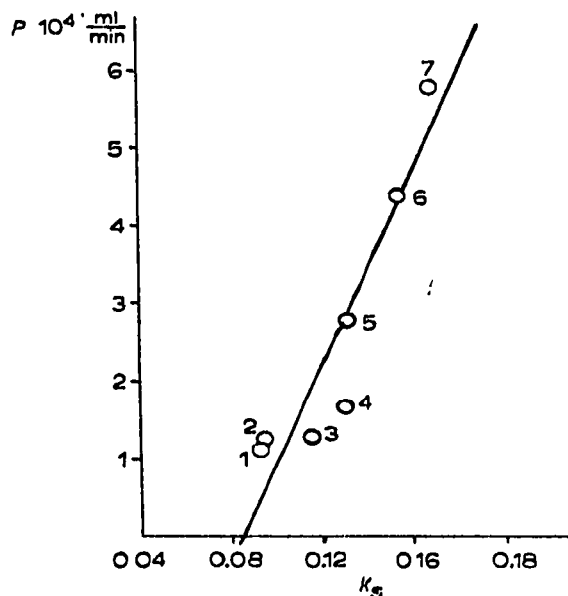

Fig. 4. Capacity dependence on the selectivity factor. Mixtures separated: 1 = carbon tetrachloride–benzene; 2 = carbon tetrachloride–cyclohexane; 3 = chloroform–cyclohexane; 4 = benzene–heptane; 5 = chloroform–cyclohexane; 6 = carbon tetrachloride–dichloroethane; 7 = heptane–methyl cyclohexane.
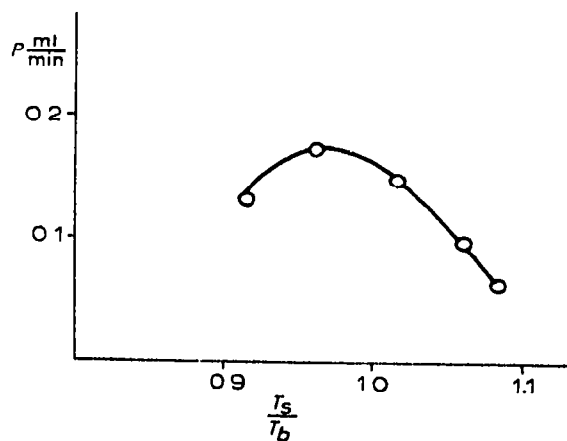
Fig. 5. Capacity dependence on column temperature. Mixture of hexane and cyclohexane, stationary phase—dinonyl phthalate; column diameter 30 mm. T_s, column temperature; T_b, boiling point of the mixture.

eters on the capacity. In cases where experimental parameters affect the distribution factor, such a consideration becomes more difficult.

In Fig. 5 are given the experimental data on the effect of temperature on the capacity. Maximum capacity is obtained at a temperature close to the boiling point of the mixture.

In conclusion, the possibility of quantitative estimations by means of eqn. 8 is considered. The ratio between K_m for the preparative column used, 14 mm in diameter, and that for the analytical column of the Griffin chromatograph was determined initially. For various hydrocarbons and chlorohydrocarbons, this ratio differed by not more than 30% and on the average was equal to 9.3 when using silicone rubber SKTFT -50 and silicone oil 2a/300 as the stationary phases. The capacity was calculated for the mixture of benzene and cyclohexane using dinonyl phthalate as a stationary phase. The values of a and K_m were determined on the analytical column as $a = 1.42$ and $K_m = 35$, from which, using the ratio 9.3, the K_m value for the preparative column was calculated. H_0 was determined by introducing 5 μl of the mixture into the preparative column. Calculated by formula 8, with $R = 1.9$ and $W = 230$ ml/min the capacity proves to be 3.34 ml vapour/min, the experimental value being 3.8 ml/min. For the mixture of benzene and heptane, the capacity calculated in a similar way for $R = 1.5$ and $W = 230$ ml/min was 2.4 ml vapour/min; the experimental value was 1.6 ml/min. Thus, eqn. 8 can apparently be used for semiquantitative evaluation of the capacity.

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