

## SCALE-UP OF GAS CHROMATOGRAPHY COLUMNS

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It is known that retention time usually passes through a slight minimum and then increases linearly with increasing sample size for compounds which produce ideal symmetrical peaks<sup>1</sup>. This is caused primarily by the increased band width at larger sample sizes. This effect can be overcome by using larger diameter columns which allow proportionally greater amounts of sample to be contained in the same band width obtained with the smaller columns. It has been observed that sample size may be quadrupled as column diameter is doubled if the length is increased by 450%<sup>2</sup>. Increasing column length by a factor of three, all other conditions remaining the same, has resulted<sup>3</sup> in tripling the amount of sample that could be satisfactorily separated.

BEROES<sup>4</sup> observed that increasing the column diameter at constant linear carrier gas velocity resulted in increased efficiency, or lower values of HETP, the height equivalent to a theoretical plate. He proposed that the effect of channeling along the walls decreases with increasing internal column diameter. This indicates that the column flow patterns, and especially the wall effect, are significantly altered in large columns. He also observed that as column diameter increases, the retention time decreases sharply if the volumetric carrier gas flow rate is kept constant. GRANT AND VAUGHAN<sup>5</sup> found that the carrier gas flow rate must be increased in proportion to the increased cross-sectional area if the retention times were to remain the same.

The amount of a sample whose components boil approximately 1° apart that can be completely resolved has been shown to be approximately one-fourth the amount that can be separated if the components differ in boiling points by 10 to 20°<sup>3,6</sup>. In both cases, the columns were deliberately overloaded to leave only a small time interval between each component.

DIMBAT, PORTER AND STROSS<sup>7</sup> observed that the slight loss in efficiency caused by increasing the column diameter from 7 to 42 mm was almost completely offset by an increase in column length of less than 50%.

KIRKLAND observed that for a limited number of systems, there was no difference in efficiency when the column diameter was increased from 4.75 to 31 mm if comparable operating temperatures were used. He adjusted the operating temperature of the larger column to a value which gave the same retention times as obtained with the smaller column.

For small samples, 2  $\mu$ l or less, KIRKLAND used a sample vaporizer 50–75° above the boiling point of the highest boiler in the sample. For 10  $\mu$ l samples, it was necessary to increase the vaporizer temperature to a level 100–150° above the boiling

temperature of the highest boiler to ensure that instantaneous volatilization during the 5-7 sec required for injection. POLLARD AND HARDY<sup>8</sup> have found that the effect of a ten-second sample injection period causes a change in HETP of only 1% as compared to plug injection.

These differences in experimental results indicate that the efficiency of separation cannot be attributed to particle size and weight ratio of substrate to support, but must also be some function of the column diameter and length and other factors associated with them. With columns of a given length, efficiency can be radically affected by changes in the porosity of the packing, velocity and temperature gradients across the column, and by channeling caused by poor sample injection and distribution techniques.

It is known that chromatographic columns operate most efficiently when the sample is distributed in a very narrow band as it enters the column, *i.e.*, efficiency increases as the injection approaches plug flow. As the column diameter is increased, the problem of maintaining plug injection becomes increasingly difficult. GOLAY<sup>9</sup> has shown that proper design and location of "distribution plates" for large diameter column can, to some extent, prevent the loss in efficiency usually encountered when scaling up analytical columns to preparative size. These plates tend to greatly reduce channeling and to flatten the velocity profile and so reduce leading and tailing.

The temperature gradients in an analytical column of small diameter operated in a constant temperature bath are quite small at low flow rates, and increase with flow rate. With small samples in such columns operated with a low carrier gas flow rate, changes in the temperature gradients caused by the heats of adsorption and desorption of the sample components should be small. With large samples in columns of large diameter, the adsorption and desorption heat effects may become large because of the wide solute band widths usually encountered in such systems. If this is the case, the temperature profiles will be distorted as the rate of heat exchange between the column and the surrounding constant temperature medium is slower than that for small columns at the same linear carrier gas flow rate. The result is that the solute is distributed in a non-isothermal band which becomes progressively more distorted as the band moves down the column. In the design of the Beckman "Mega-chrome" unit, an attempt has been made to overcome this problem by the use of several small columns operated in parallel for the separation of large (10-50 g) samples. An alternative to multiple column operation might be to pack the annular space between two large, concentric tubes or pipes, *i.e.*, pack the annulus between a 2-in. and a 4-in. tube and have the constant temperature medium circulating on both sides of the column. Another alternative might be the use of heat conducting rods inserted axially in the column to break up the temperature profiles in large diameter columns by acting as heat sinks.

The modified Reynolds number, based on average particle diameter and superficial vapor velocity,

$$N'_{Re} = \frac{d_p V_o \rho}{\mu}$$

was used in this work as it has been found to be an excellent method for correlating data to show the physical effects of varying, either independently or collectively, the velocity, viscosity, density, and packing particle size on fluid flow. Its usefulness as a

design factor in the construction of preparative-scale gas chromatography columns is a natural extension from common chemical engineering design methods for packed absorption towers, fixed-bed catalytic reactors, etc. The study reported here was designed to determine the effect of varying the modified Reynolds number and the ratio of column diameter to particle diameter,  $Z$ , on retention time for samples of constant size at moderate carrier gas flow rates. For this work, the density and viscosity of the carrier gas were used at average column absolute pressure as being representative of the bulk gas phase.

## EXPERIMENTAL

### *Apparatus*

The columns used consisted of a 129.4 cm packed length of borosilicate glass tubing surrounded by a vapor jacket composed of a 135.0 cm section of 5.1 cm internal diameter glass tubing. The column assembly has already been described<sup>1</sup>. The column diameters tested were 3.1, 4.6, 7.0, 9.0 and 18.1 mm. The thermal conductivity cell, recorder, and flow control system were as previously described.

### *Test mixtures*

Test mixtures were prepared as follows. No. 1: 2-butanone, ethoxyethane, 2-propanone, and 2-(1-methylethoxy)-propane. No. 2: methanol, ethanol, 2-propanol, 1-propanol, 2-methyl-2-butanol, and 2-butanol. No. 3: ethyl formate, vinyl acetate, ethyl acetate, and methylethyl acetate. The choice of components for the test mixture was governed by the desire to have short total analysis times. The purity of the sample components was the highest normally available. Each mixture consisted of an equivolume mixture of the listed components.

### *Procedure*

The column packing was 35 g of dibutyl phthalate per 100 g of —48 + 65 Tyler standard mesh type C-22 Johns-Manville firebrick. The method of packing preparation and system operation were as previously described. The columns were maintained at 98.6° by refluxing water in the vapor jacket. Samples were injected into the system through a self-sealing rubber serum cap. The sample size used in this work was 10  $\mu$ l. Sample injection and vaporization was complete within 2 sec or less.

## RESULTS AND DISCUSSION

### *Flow rate changes*

The 3.1, 4.6, 7.0, and 9.0 mm inside diameter columns were tested at carrier gas flow rates at 5.0, 10.0, 19.6, 36.5, 58.5, and 78.0 ml of helium per min. The 18.1 mm inside diameter column was tested at flow rate of 5.4, 32.5, and 78.0 ml/min. Inlet pressure to all the columns except the 18.1 mm I.D. column was 20 p.s.i.g. For the latter column, the inlet pressure required was 30 p.s.i.g.

For these runs the ratios:

$$Z = D_T/d_p$$

of column diameter to average particle diameter were 12.3, 18.3, 27.8, 35.7, and 71.8

in order of increasing column diameter. The average particle diameter was 0.25 mm which corresponds to the -48 + 65 mesh Tyler standard screen fraction. The retention time is greatly dependent on the Reynolds number (or at least velocity) for the work done at the two lowest values of  $Z$ . At the two highest values of  $Z$ , the retention time is only slightly effected by changes in the Reynolds number. Under these conditions a plot of corrected retention time ( $T_R^\circ$ ) vs.  $N'_{Re}$  gave straight, nearly horizontal

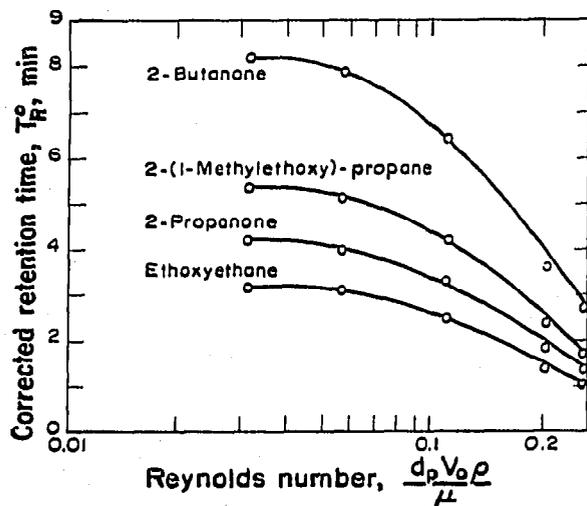


Fig. 1. Effect of modified Reynolds number on corrected retention time. Particle diameter: 0.25 mm (-48 + 65 Tyler standard mesh). Column diameter: 3.1 mm.

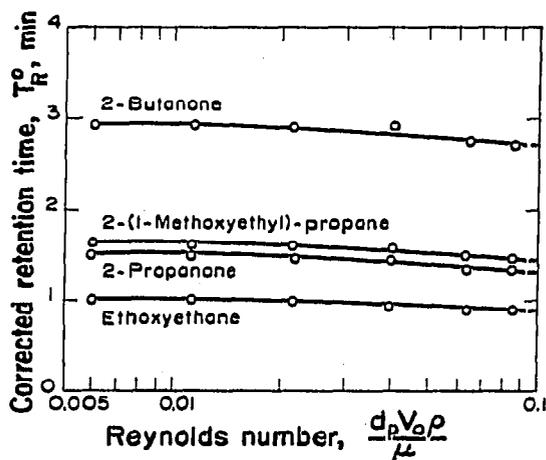


Fig. 2. Effect of modified Reynolds number on corrected retention time. Particle diameter: 0.25 mm (-48 + 65 Tyler standard mesh). Column diameter: 7.0 mm.

lines which were approximately parallel. Representative data obtained with the ether-ketone test mixture (No. 1) under the above conditions is presented in Fig. 1 for  $Z = 12.3$ . The data points in this figure are numerical averages of triplicate observations. Deviations between observations were less than 0.8% in all cases. As

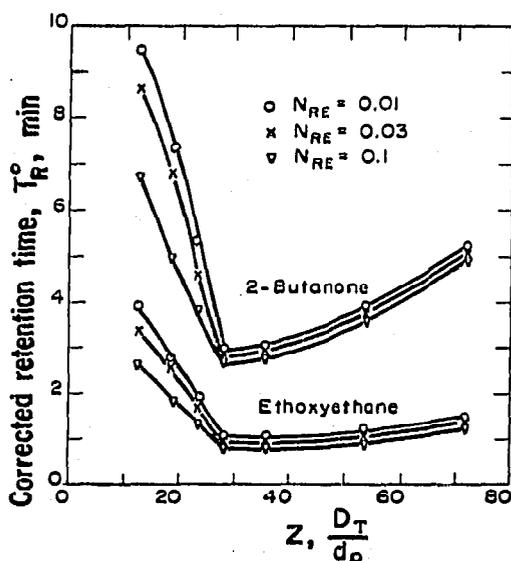


Fig. 3. Effect of column to particle diameter ratio on corrected retention time. Particle diameter: 0.25 mm. Column diameter: variable.

the average column pressure increased with increasing flow rate the retention times plotted have been corrected for the compressibility of the vapor phase by the method of JAMES AND MARTIN<sup>10</sup>. The case where  $Z = 27.8$  seems to be a transition point (Fig. 2). The curvature, unlike that exhibited in Fig. 1, is very slight. The transition produces a definite minimum value of  $T_R^\circ$  when plotted against  $Z$  for different Reynolds numbers. This is shown in Fig. 3 for 2-butanone and ethoxyethane. The only explanation that presented itself for these minima was that the wall effect becomes appreciable at the lower  $Z$  values, resulting in a widening of the solute band. This increase in band width may be caused by the fact that the velocity at a point approximately one particle diameter from the column wall may be as much as 100% greater than the velocity of the column<sup>4,11,13</sup> because of radical porosity changes. The result is increased channeling of the flow as the column diameter is decreased as is indicated by the change in the curvature on the left. As  $N'_{Re}$  increases, the minimum value of  $T_R^\circ$  decreases as would be expected.

### Particle size effects

In order to be sure that the curves in Fig. 3 were not peculiar to the system used (test mixture 1 on the -48 + 65 dibutyl phthalate column) additional work was done using test mixtures 2 and 3. For this work, the column internal diameter was held constant at 4.6 mm and the -28 + 48, -48 + 65, -65 + 100, -100 + 150, and -150 + 200 mesh Tyler standard fractions of crushed C-22 firebrick were used to prepare a series of packings, each having 35 g dibutyl phthalate per 100 g brick. Similar packings using dibutyl sebacate were also prepared in these size fractions. When the corrected retention times were plotted *vs.*  $Z$  for  $N'_{Re} = 0.01$  and 0.1, the curves were found to have minimum values of  $T_R^\circ$  at  $Z = 26$  to 29 for the components of test mixtures 2 and 3 in the dibutyl phthalate packings. This work was duplicated for the same test mixtures in the dibutyl sebacate columns. Minimum values of  $T_R^\circ$  were found at  $Z = 24$  to 27. For both these two series of tests, the column temperature was 98.6°. The same flow rates as used in the ether-ketone phase of the work were used for the 4.6 mm internal diameter column just described.

Further work was done using the -28 + 48 Tyler mesh dibutyl phthalate packing in each of the 5 columns. For these runs the column inlet pressure was 30 p.s.i.g. in all cases. The flow rates tested were the same as those used for the initial work using test mixture No. 1. Minimum values of  $T_R^\circ$  were found at  $Z = 20$  to 25.

The left branch of the curves in Fig. 3 may be explained by the fact that the porosity increases near the column wall. As the column diameter was increased, the proportions of the relatively porous area to the total column cross-sectional area decreased, causing a decrease in the average column porosity. The limiting retention time  $T_R^\circ$  can be calculated<sup>12</sup> from:

$$V_R^\circ = V_o + KV_s = FT_R^\circ \quad (1)$$

or:

$$T_R^\circ = V_o/F + KV_s/F \quad (2)$$

As the temperature is constant the partition coefficient  $K$  should not change. Decreasing in the average column porosity by increasing the column inside diameter caused a decrease in the area available for the gas phase in any cross-section. Although

the total amount of liquid phase present is increased by decreasing the porosity in this manner this should not have much influence on the retention time for work done using a given particle size since the solubility of the sample in the substrate is not generally a limiting factor in the case of high substrate to brick weight ratios such as used in this work.

With increasing average column pressure the volume of gas in the column at standard conditions increases, while the volumetric flow rate remains constant. This would cause an increase in the retention time. It is suggested that above  $Z$  values of approximately 25 to 30 the effect of increased average column pressure will overcome the effect of changes in the average column porosity. The result is an increase in retention time as seen in the right branch of the curves in Figs. 3 and 4.

The shift in the location of the minima illustrated in Fig. 4 when using different

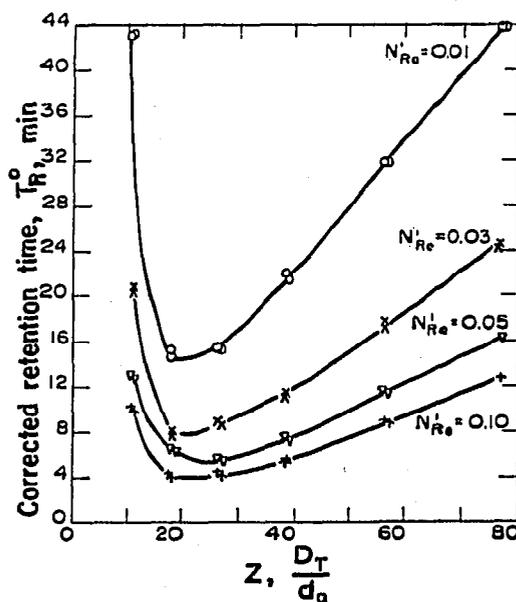


Fig. 4. Effect of column to particle diameter ratio on corrected retention time for ethanol. Particle diameter: variable. Column diameter: 4.6 mm.

particle diameters in the 4.6 mm column compared with those obtained using a constant particle size in columns of different diameter is undoubtedly due to the change of the thickness of the substrate film caused by changing the particle diameter while holding the ratio of substrate to brick constant. These changes in liquid film thickness are not too large as the surface areas of the packings, as determined by the Johns-Manville Corp., Mannville, N.J., by the Brunauer-Emmett-Teller method were: 4.0, 3.2, 3.0, 3.0, and 2.3 m<sup>2</sup>/g for the — 28 + 48, — 48 + 65, — 65 + 100, — 100 + 150, and — 150 + 200 Tyler standard screen fraction, respectively.

#### Temperature effects

The effect of changing the Reynolds number by changing the operating temperature has been investigated using room temperature, 65°, 98.6°, and 127.5° for the — 48 + 65 mesh dibutyl phthalate and dibutyl sebacate packing in the 4.6 mm diameter column at flow rates of 5.0, 27.5, 50.6, 61.8 and 76.5 ml helium per min. In

all cases when corrected retention time was plotted vs. log Reynolds number, straight lines were obtained as would be expected.

### CONCLUSIONS

From the data collected it appears that the contribution of the wall effect to retention time is a general phenomenon. It is also concluded that large scale chromatography columns can be prepared which will operate at maximum efficiency and minimum retention time if the ratio of column diameter to particle diameter is maintained at approximately 25. This is in close agreement with a  $Z$  value of 30 obtained by SCHWARTZ AND SMITH<sup>11</sup> using various packing sizes and shapes in 2 to 4 inch pipes. Further work is in progress and will be reported later.

### ACKNOWLEDGEMENT

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### SUMMARY

The effect of the modified Reynolds number,  $N'_{Re}$ , and the ratio of column diameter to support particle diameter,  $Z$ , have been studied in 5 column sizes and 5 particle sizes at 6 flow rates, for several test mixtures of oxygenated aliphatics. The results indicate that minimum values of the pressure-drop-corrected retention time,  $T_R^\circ$ , will be obtained at  $Z$  values of 20-29, with an average value close to  $Z = 25$ .

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