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Empirical Correlations for Pressure Drop Across A Chromatographic Bed Packed with A Compressible Packing

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ABSTRACT

Experiments were done to obtain a correlation between pressure drop across a chromatographic bed packed with a compressible packing, Sephadex G100, and other measurable parameters such as flowrate, column length and diameter, particle size, and permeability. The pressure drop across the bed is obtained by subtracting the extracolumn pressure drop from the operating pressure drop. It was found that the pressure drop increased nonlinearly as the flowrate increased. There is a critical flowrate after which the pressure drop increases infinitely. The pressure drop was also found to be dependent on the column diameter within the range tested. The data were fitted well with an equation similar to the Blake-Kozeny equation but with an exponential term and a critical factor included.

ABSTRAK

Uji kaji telah dijalankan bagi mendapatkan persamaan yang menghubungkaitkan susutan tekanan bagi turus padat yang mengandungi Sephadex G100, sejenis padatan boleh mampat, dengan kadar alir, garis pusat turus, panjang turus, saiz zarah, dan penelapan. Susutan tekanan yang digunakan didapati setelah mengambil kira susutan tekanan yang bukan dari turus terpadat. Data menunjukkan yang susutan tekanan adalah tidak linear dan apabila sampai pada satu kadar alir genting, susutan tekanan meningkat ke infiniti. Susutan tekanan telah didapati juga bergantung kepada garis pusat turus di dalam julat yang dicuba. Satu persamaan yang hampir serupa dengan persamaan Blake-Kozeny tetapi mengandungi eksponen dan juga faktor genting telah digunakan untuk menghubungkaitkan data yang diperolehi.

INTRODUCTION

Chromatography has been used widely as a separation tool for enzymes and other biological molecules. Most of these macromolecules are relatively delicate structures and thus cannot be chromatographed on rigid hydrophobic supports without any significant loss of activity. As a result most of the separations were done using soft packings which are easily compressed. This compressible nature in turn causes many complications in scale-up effort (Janson 1974).

One of the limitations in using compressible packing is the inability to use large flowrates. Kelley et al. (1986) pointed out that even a slight difference in the degree of compressibility can cause up to four-fold difference in productivity. In order to scale-up such a compressible system, it is important to find a correlation between the pressure drop and measurable parameters such as velocity, column diameter and length, and particle diameter. It should also be pointed out that as the column diameter increases, the wall support diminishes. This effect has to be accounted for in the correlation. The purpose of this work is to find the correlation mentioned above.

BACKGROUND

For rigid packing, the linear Blake-Kozeny equation has been used successfully (Bird et al 1960).

$$\Delta P = \frac{\mu \upsilon_o L}{k d_p^2} \tag{1}$$

where

$$k = \frac{\varepsilon^3}{[150(1-\varepsilon)^3]} \tag{2}$$

The wall effect is taken into account when the ratio of column diameter to particle diameter is less than 50 to 1 (Mehta and Hawley 1969). However, for compressible packing, the correlation between flowrate and other measurable parameters has been found to be non-linear (Joustra et al 1969). This is due to the effect of compression which will reduce the porosity inside the bed and eventually clog the system. This will lead to a very high pressure drop. There have been several attempts to try to find the appropriate correlations (Joustra et al 1967; Davies and Bellhouse 1989). One of the shortcomings of the previous studies is the use of an operating pressure-drop which includes the extracolumn pressure drop, not the pressure drop across the chromatographic bed itself. Since the extracolumn pressure drop is different for columns with different diameters and lengths, its inclusion will not give accurate correlation of the pressure drop.

An analysis of the forces acting on a compressible particle in the column will show the effect of the wall and flow on the overall pressure drop across the column (Janson and Hedman 1982). Figure 1 shows the force distribution on a spherical particle that is falling in a liquid. The force which is due to the velocity in the pores between the particles (u) is pushing the particle downward and is equal to the fric. The compression caused will increase the shape factor and decrease the bed porosity. Both effects will contribute to a much higher pressure drop aross the bed. The presence of the wall will counteract the compression forces. As shown in Figure 2, F_1 represents the summed liquid frictional forces pushing particle A and all the particles on top of A downward. F_1 is distributed in n other directions to a number of particles that support particle B. One component is F_2 acting on a particle contacting the column wall. The vertical component of F_2 is balanced by the friction at rest resulting from the wall contact and the vertical component F_3. Thus, the push on particle D is reduced by the wall friction. However as the column diameter increases, the support provided by the column will eventually diminishes and the pressure gradient through the bed is due to the drag force only.

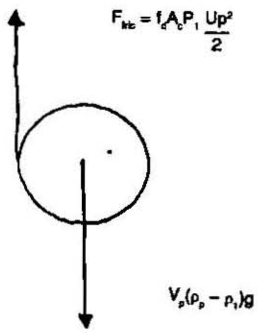

FIGURE 1

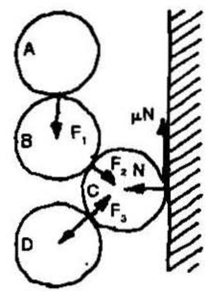

FIGURE 2

Davies and Bellhouse (1980) have derived the pressure drop correlation from theoretical consideration for short column limit. However, for long and moderate column, no analytical solution is possible and thus numerical calculation is required. For design purpose, empirical correlations will be much more desirable since it will reduce the complication during scale-up analysis.

EXPERIMENTAL METHODS

The overall system for the experiments is shown in Figure 3. Three columns with diameters of 1.6 cm, 2.6 cm, and 5.0 cm were used (corresponding to the columns XK16, XK26, and XK50 respectively from Pharmacia. Three displacement pumps (Minipump, Milton Roy Co. with ranges of 0.0 to 2.67 ml/min and 0.767 to 7.67 ml/min, and Masterflex, Cole-Palmer Co. with ranges of 10.0 to 100 ml/min) were used to pump the eluent through the system. The eluent used was distilled water which was degassed before each run.

Pressure drop across the column is measured using a pressure transducer, Viatran differential pressure transducer model 123, with range of 0 to 125,000 dynes/cm^2. The transducer is attached to a regulated power source and to a meter (Keithley model 197 digital multimeter) from which voltage can be read.

The packings used are Sephadex G100 regular and superfine, made by crosslinking dextran with epichlorohydrin (Pharmacia 1985). These packings have been used quite successfully for fractionating large peptides and globular proteins such as plasma proteins (Flodin 1962). These gels are very hydrophilic and thus swell very well in water and electrolyte solutions. Table 1 shows an analysis of wet and dry particle diameters for the packings obtained using dark-field microscope.

The measured pressure drop includes the extracolumn pressure drop which comes from the tubing, plunger, and net ring. The extracolumn pressure drop was obtained for each column by measuring the pressure drop

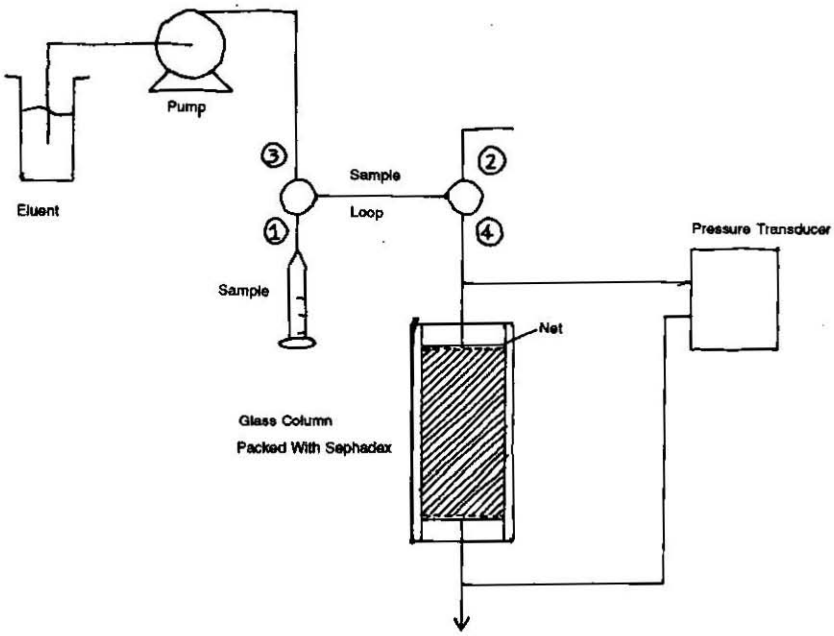

FIGURE 3

TABLE 1. Average values for the particle diameters

	Sephadex G100 Regular		Sephadex G100 Sperfine	
	Dry	Wet	Dry	Wet
Mean (μm)	53	157	24	88
Minimum (μm)	15	63	8	26
Maximum (μm)	96	307	53	200
Median (μm)	51	149	22	78
Standard Deviation (μm)	17	48	10	36

across an empty column (without packing). The pressure drop across the empty column is negligible compared to the pressure drop of the tubing, expansion and contraction, and the net ring. The pressure drop across the bed is obtained by subtracting extracolumn pressure drop from the measured pressure drop. The extracolumn pressure drop accounted for 30% -70% of the total pressure drop depending on the columns and type of tubes used (Abdul Wahab Mohammad 1991).

RESULTS AND DISCUSSION

EXPERIMENTS CARRIED OUT WITH SEPHADEX G100 REGULAR

Experiments at Different Diameters, Constant Length Figure 4 shows the plot of pressure drop vs velocity for all three column diameters. Two important observations from this plot are the nonlinear relationship between pressure drop and velocity which includes the existence of a critical velocity, and the dependence of pressure drop on column diameter. These two phenomena are caused by two different effects. The nonlinearity is believed to be caused by the fact that particles at the bottom of the column are much more deformed than those at the top of the column. As the flow rate increases, these severely deformed particles reduce the porosity at the bottom level which resulted in increasingly high pressure drop until the critical velocity at which the porosity becomes really low and the pressure drop increases infinitely. This explanation follows that proposed by Ladisch and Tsao (1978) for ion exchange resins. An additional observation to support this is that the column length did not change by much when the flowrate is close to the critical flowrate. That means the particles could not be compressed further, yet the pressure drop increased significantly.

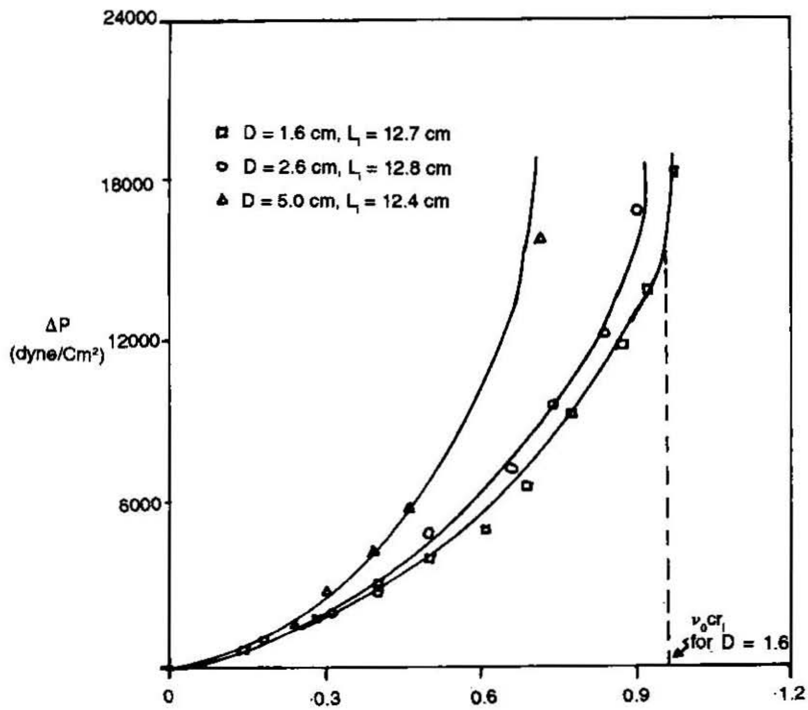

FIGURE 4

The dependence of the pressure drop on column diameter can be explained by the presence of wall support. As the flowrate increases, the particles are deformed from a spherical shape to probably an egg-like shape. This in turn, creates a fore which will be balanced by the support from the wall. As the column diameter increases, the wall support diminishes. The loss of support will reduce the porosity which cause the pressure drop to be higher at the same flowrate. Figure 4 shows that at a constant flowrate, the pressure drop for the 5 cm diameter column is always higher than that for the 2.6 cm column and 1.6 cm diameter columns. The difference is smaller between the 2.6 cm and 1.6 cm column. The wall effect mentioned here is different than those observed with rigid packings (Cohen and Metzner 1980). For rigid packings the wall effect is significant only when the column diameter to the particle diameter ratio is less than 50 to 1.

Experiments at Varying Lengths, Constant Diameter These experiments were done to investigate the effect of column length on the pressure drop. Only the 2.6 cm diameter column has a long enough plunger to allow for four different bed lengths. Figure 5 shows the plot of pressure drop vs velocity for all the four cases. Based on the Blake-Kozeny equation, by doubling the length, the pressure drop will also double. However with compressible packings, this is not the case. As the length increases, the pressure drop increases much faster than linearly. This can be attributed to the fact that the longer bed will put more weight on the particles at the bottom. Coupled with the compression force from the flow, the particles at the bottom will deform faster and thus the pressure drop increases at a much faster rate.

EXPERIMENTS CARRIED OUT WITH SEPHADEX G100 SUPERFINE

Experiments at Different Diameters, Constant Length Similar experiments as with G100 regular were done with G100 superfine. G100 superfine is a

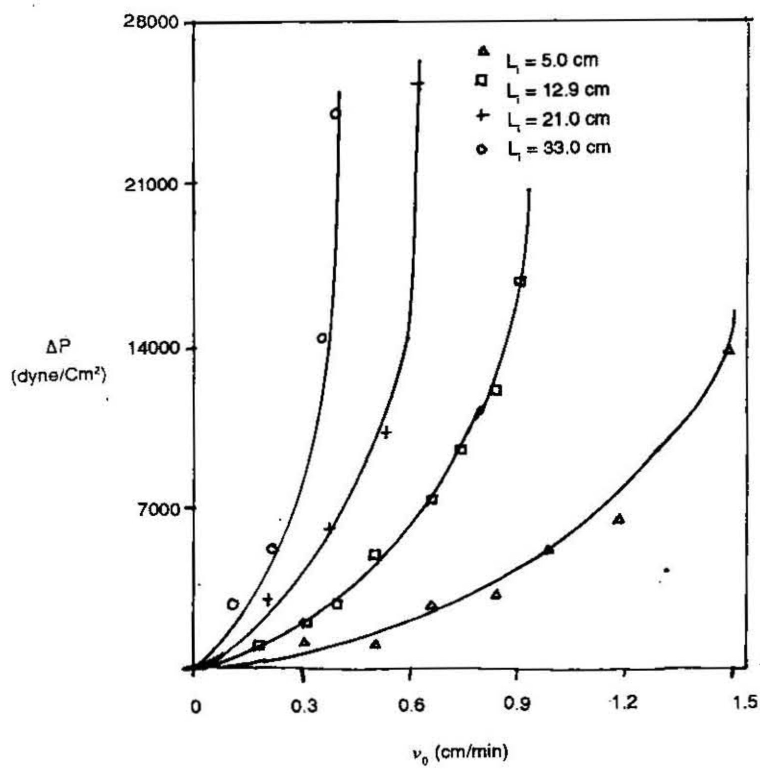

FIGURE 5

packing with an average particle diameter about half of that for G100 regular. As Figure 6 shows, the pressure drop dependence on column diameter is small. It is possible that the small diameter particles used diminishes the wall support that forms when the particles were compressed. The ratio of the column diameter to particle diameter is now approximately doubled which makes it harder for the wall to support the particles.

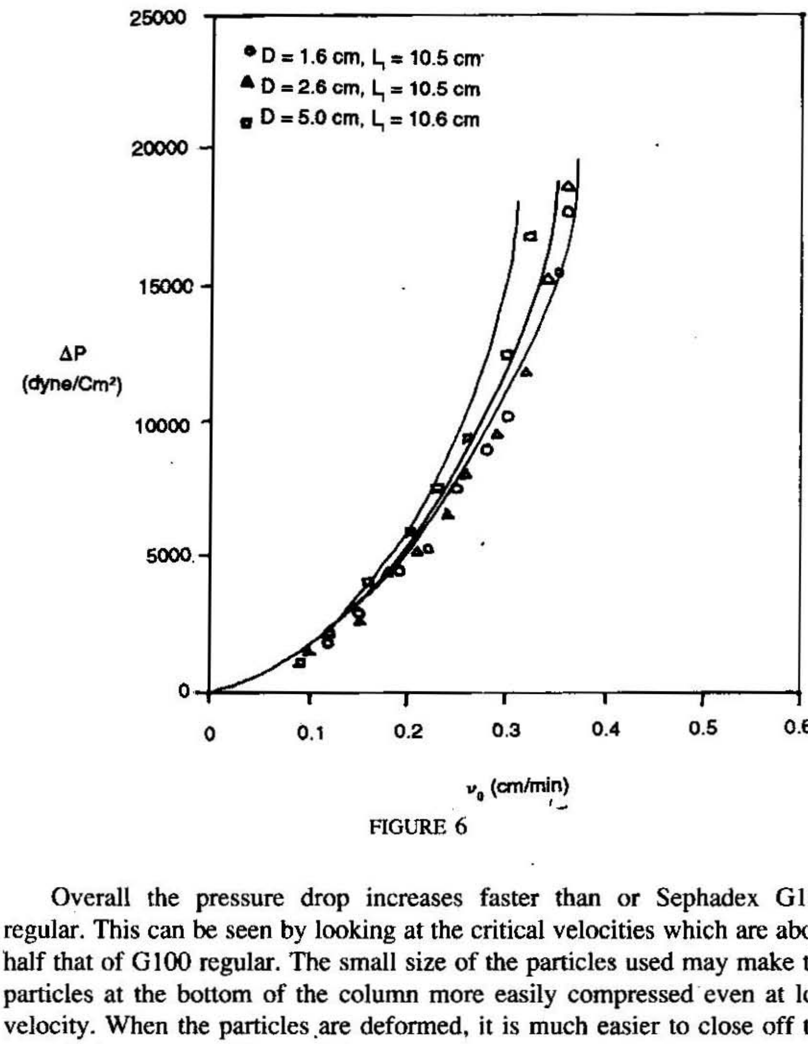

FIGURE 6

Overall the pressure drop increases faster than or Sephadex G100 regular. This can be seen by looking at the critical velocities which are about half that of G100 regular. The small size of the particles used may make the particles at the bottom of the column more easily compressed even at low velocity. When the particles are deformed, it is much easier to close off the pores in between smaller particles than larger particles because the pores are smaller. This would result in significantly higher pressure obtained.

Experiments at Varying Lengths, Constant Diameter Again these experiments were done to investigate the effect of length of the pressure drop. Figure 7 shows the plot of pressure drop vs velocity for column 2.6 cm diameter. Again the increase in pressure drop is more than double even when the length is only two times longer. Also it is much more difficult to achieve equilibrium for smaller particles since the critical velocity is low.

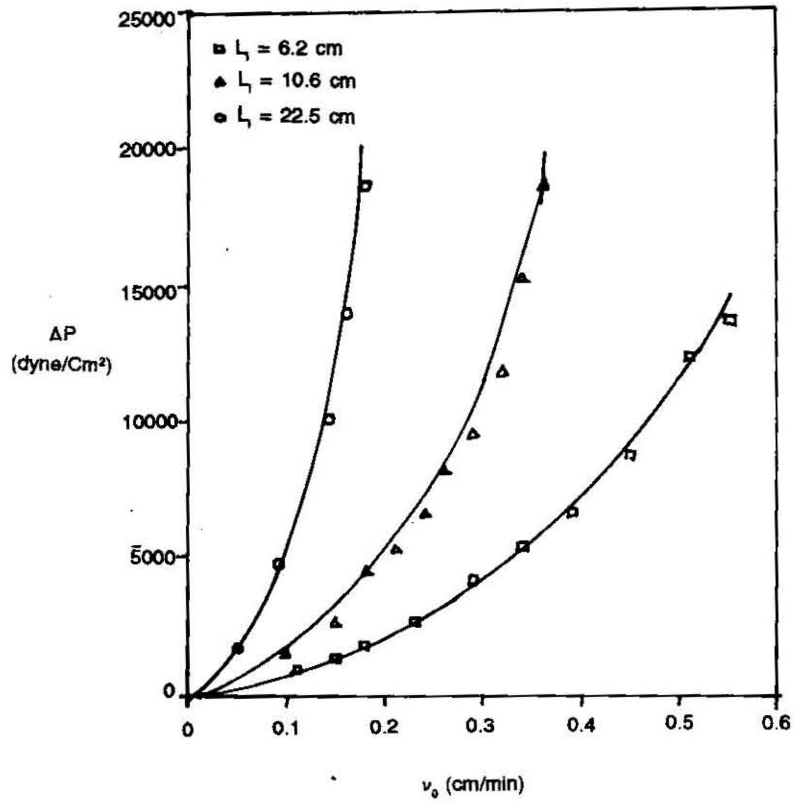

FIGURE 7

MODELLING THE PRESSURE DROP

In trying to model the pressure drop data, a correlation that relates the pressure drop to measurable parameters such as velocity, column length, permeability, column diameter, and particle diameter should be the objective. With that in mind, the following equation has been found to fit the data very well.

$$\Delta P = \frac{\mu \upsilon_o L}{k_o d^2_{p,o}} \phi \exp(a \upsilon_o L) \tag{3}$$

where

$$\phi = 1 + \frac{1}{C_1(1 - \upsilon_o L/\upsilon_{o,cri} L)} \tag{4}$$

$$k_o = \frac{\varepsilon^3_o}{150(1-\varepsilon_o)^2} \tag{5}$$

Equation 2 is similar to the Blake-Kozeny equation but with an exponential term and a critical factor, ϕ, added. The "a" term in Equation 3 was found to correlate linearly with the ratio of column diameter to initial length D/L_i. Note that L_i is the length of the bed at the initial stage when there is no flow. L is the bed length after the compression had taken place at a particular velocity υ_o. The term ϕ takes into account the critical velocity at which the pressure drop increases infinitely. C_1 is a constant that will make ϕ significant only when υ_o is close to the critical value. A value of 200 for C1 was found to be adequate. It was found that $\upsilon_{o,cri}L$ can be correlated to the ratio D/L_i. This is why $\upsilon_{o,cri}L$ is used in Equation 4. The permeability term at the initial stage when there is no flow is k_o. As the flowrate increases, the permeability will change and this is accounted for in the exponential term. Similar reasoning is applicable to the particle diameter. The initial particle diameter $d_{p,o}$ is the diameter measured when the particle is at equilibrium with the solvent. However as the flowrate increases, the particle will be deformed and this will change the particle diameter. This change is also being taken into account by the exponential term.

For k_o it was assumed that initially, the particles are spherical and thus they were packed in a way that will give equal void fractions independent of column diameter, length, or particle diameter. The reported value for the initial void fraction for Sephadex G50 particles, which are also quite compressible, ranges from 0.45 - 0.47 (Edwards and Helft 1970). Eventhough the particles used are Sephadex G100 particles, the initial void fraction should not differ by much since initially the particles are spherical. An average value of 0.46 was used in modelling the data. This value is substituted into equation 5 to obtain the initial permeability k_o. Average values for the particle diameters as shown in Table 1 were used.

The experimental data were fitted to Equation 3 to obtain the value for "a". The "a" values can be correlated to the ratio of column diameter over the initial length, D/L_i. Figure 8 and 9 show the plots of the constant "a" vs D/L_i, and $\upsilon_{o,cri}L$ vs D/L_i and their fitted equations respectively. The fitted pressure drop data are shown in Figure 4, 5, 6, and 7. For both Sephadex G100 regular and superfine the data are correlated well with Equation 3.

CONCLUSIONS

For compressible packings as shown with Sephadex G100,t he pressure drop correlation is nonlinear. At the critical velocity, $\upsilon_{o,cri}$, the pressure drop did not equilibrate and increase infinitely. Experiments with different column diameters showed that the pressure drop is dependent on the column diameter within the limit tested. The pressure drop increases as the column diameter increases. Experiments with varying lengths and constant diameter showed that when the column length is doubled the pressure drop increases by more than twice. With smaller particle sizes, the pressure drop dependence on column diameter is smaller, however, the pressure drop increases much faster. Using Equation 3, the data were correlated well as functions for flowrate, column length and diameter, particle size and permeability.

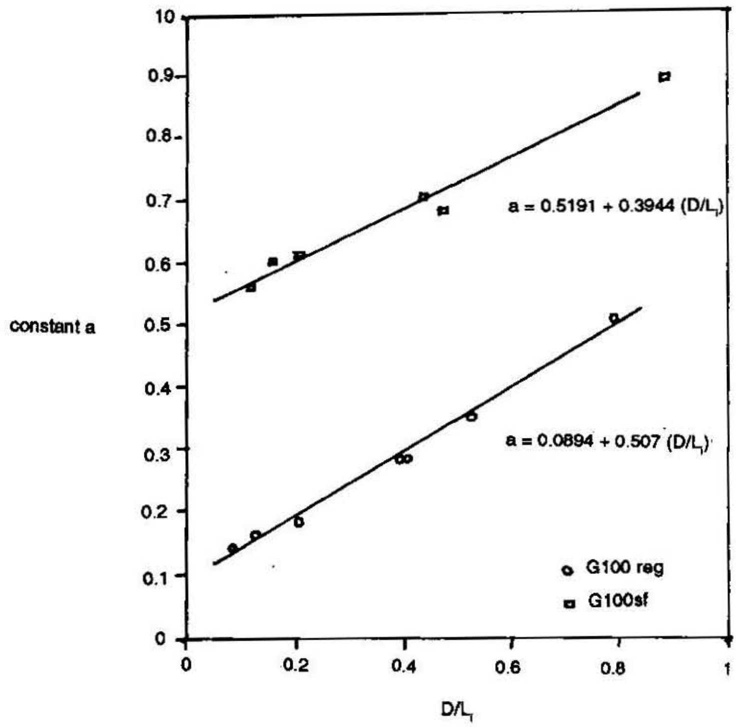

FIGURE 8

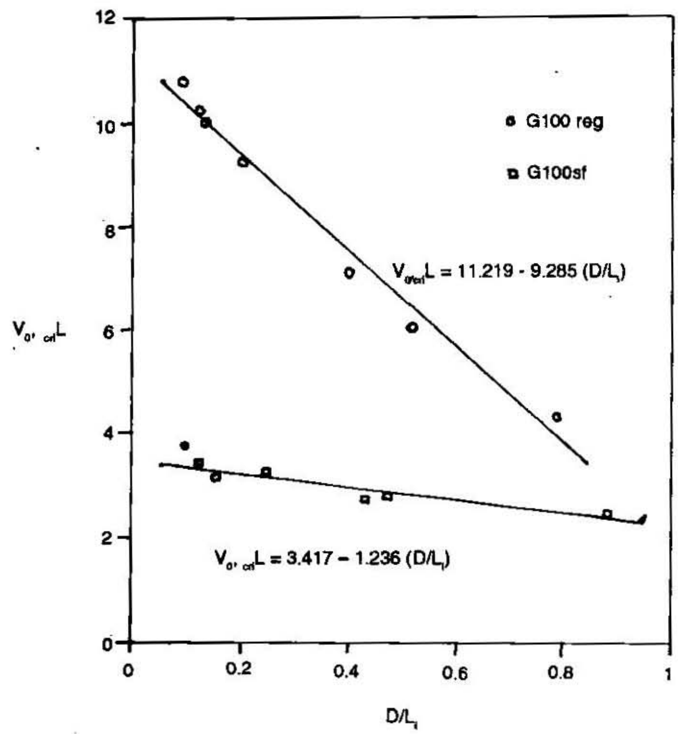

FIGURE 9

Future works should be done on different packings with different degree of compressibility and also on larger column diameter to see whether the dependence on column diameter still hold. Only then, it is possible to correlate "a" to the degree of compressibility and column diameter.

NOMENCLATURE

a	as defined by Equation 3
C_1	constant in Equation 4
d_p	particle diameter, cm
k	permeability constant
k_o	initial permeability constant
L	column length, cm
υ_o	superficial velocity, cm/s
$\upsilon_{o,cri}$	critical superficial velocity
ΔP	pressure drop, dynes/cm2
ϵ	interparticle void fraction
ϵ_o	initial interparticle void fraction
μ	viscosity, g/(cm s)
ϕ	as defined by Equation 4

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