PRESSURE DROP ACROSS COMPRESSIBLE BEDS

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Columns with fixed beds of immobilized enzymes or other proteins are commonly used in affinity chromatography and as reactors for continuous operation. Most carrier particles for protein immobilization are deformable or compressible by application of pressure. For non-compressible beds at low Reynolds-numbers, <10, the pressure drop p is a linear function of flow rate i and the flow resistance is constant. With deformable particles in fixed beds p is a non-linear function of bed height h and volumetric flow rate v (1). This is shown in Fig. 1 where the flow resistance increased with p, finally leading to instability and occlusion. It is evident that at p = 100 mbar the pressure drop increased very rapidly with the flow rate, and occlusion occurred beyond about 500 mbar. The maximal flow rate depended on h as expected. Reproducibility was difficult, depending on pretreatment and hysteresis. The flow through a compressible bed must take into account varying hydraulic radii r_h in the flow path, caused by particle deformation. The pressure drop then becomes a function of h, v, and r_h. From the law of Hagen-Poiseuille p = f(h) = (constant)(f(v)). Thus, it is possible to determine the application range of bed height, flow rate, and residence time, for a given carrier by one type of experiment, either from p = f(h) or from p = f(v). The results may be summarized through the specific flow resistance as a function of p; by analogy to filtration theory (2)
\[ \alpha = \frac{dp}{d(hw) \mu} \]  
(\text{Eq. 1})

\[ \bar{\alpha} = \frac{p}{(hw \mu)} \]  
(\text{Eq. 2})

where \( \bar{\alpha} \) is a mean flow resistance for an integral bed, \( w \) is the linear flow rate, and \( \mu \) is the viscosity. For a given \( p \) the residence time or \( h \) and \( w \) can be calculated if \( \bar{\alpha} \) is known as a function of \( p \).

A qualitative understanding of the observed phenomena is possible using a simple schematic model based on elastic deformable spheres as carrier particles with a modulus \( A \) defined by \( \Delta r/r_0 = A \rho \) (3). \( p = f(h) \) was calculated by approximation and compared with \( f(v) \), which was experimentally determined. The approximation was done by calculation of the pressure drop in the first layer of spheres (in a dense column packing) according to Hagen-Poiseuille such that

\[ p_1 = \frac{8 \mu \nu h_1}{(n_q \pi r_{h1})^4} \]  
(\text{Eq. 3})

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**Fig. 1.** Total pressure drop in columns with Sepharose CL 6B for different bed heights \( h \) (dp 100-200 \( \mu \)m) (experimental).