INTERACTION BETWEEN POLYSACCHARIDES AND OTHER SUBSTANCES. NON-EQUILIBRIUM CONDITIONS

B. N. Preston (Clayton, Victoria, Australia)

It is generally agreed that solutions of polysaccharides may be regarded as a model for the extracellular space of connective tissues. There is evidence which suggests that the polysaccharide chains, in the form of high molecular weight proteoglycans, entangle and form continuous three dimensional networks which may be considered as occupying the space between the connective tissue cells. Furthermore, macromolecular solutes such as polysaccharides, represent micro-heterogeneous regions in a solution. In particular, the spatial distribution of mass, charge density and mobility is very different from that found in solutions of small molecules. It is expected therefore that such microheterogeneity may play an important role in the transport properties of the solutions and hence by inference may influence diffusant behaviour in biological processes.

The dynamic interactions that occur between the migrating species and the network structure may depend upon many factors including (1) the size and shape of diffusant and (2) the concentration and molecular weight of the network forming polymer. Present studies have shown that polysaccharides (e.g. dextran) markedly retard the diffusion of various small solutes (monosaccharides, sodium ion etc.). A semi-quantitative explanation of these findings can be made in terms of the viscosity of the microenvironment or by evoking the concept of mechanical obstruction by the hydrated polysaccharide chains. Earlier studies[1,2] have shown similar retardation effects on the transport of various globular proteins and particles in solutions of hyaluronate and of sulphated proteoglycan. A theoretical treatment of this behaviour based upon obstacle hindered diffusion has been developed by Ogston, Preston and Wells[2]; its applicability to the migration of large particles however has been questioned[3].

Studies on the rotational diffusion of proteins[4] indicate that the effective microviscosity of the polysaccharides is low and support the idea that the retardation of the translational movements cannot be a microviscous effect.

The transport of assymetric or flexible macromolecules in polysaccharide solutions display complex behaviour. At low concentrations of polysaccharide, it has been shown[5] that the translational migration of linear molecules such as DNA is retarded. However, the retardation is consistent with an end-on motion. At higher concentrations of the network polymer, very marked enhancement of migration rates is observed. Detailed studies have indicated that a hydrodynamic coupling may occur between the network polymer and the migrating species but no evidence for convectional bulk flow can be found.

Changes in the configuration of flexible macromolecules caused by the presence of the polysaccharide network has been investigated by viscometry. Regarding the system as pseudo-binary, the hydrodynamic volume of the flexible polymer (e.g. polyvinylpyrollidone) displayed a ten-fold decrease with increasing concentration of polysaccharide. A quantative explanation of this decrease can be offered by a modified version[6] of the Flory theoretical discussion of the effect of a single solvent on chain configuration[7]. Similar studies on the hydrodynamic volume of compact structures, such as

albumin and collagen, in the presence of polysaccharide reveal little configurational change.

In order to clarify the situation existing in the ternary system (polymer-polymer-solvent), extensive studies on the simpler binary system (polymer-solvent) has been undertaken. Recent work[8 9] has established the relationship, $D_m = D_s(1-cv)(1+2A_2Mc+ \ldots)$, that exists between the two physically distinct coefficients required to describe the translational diffusion of molecules in solution. One of these, the mutual coefficient, D_m characterizes the relaxation of a concentration gradient whilst the other, the self, tracer or intradiffusion coefficient D_s, characterizes the random motions of an individual solute molecule. c, v, A_2 and M are respectively the concentration, partial specific volume, second virial coefficient and molar mass of the polymer. With solutions of dextran, a twenty fold difference in these coefficients is observed. It is evident that the presence of concentration gradients in the microenvironment has significant effects on the diffusional movements of polymers[9].

The importance of the above observations will be discussed in relation to biological processes.

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