INTERACTION BETWEEN POLYSACCHARIDES AND OTHER SUBSTANCES. EQUILIBRIUM CONDITIONS.

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The non-covalent interaction between polysaccharides, such as the glycosaminoglycans in the connective tissues, and other macromolecules can for convenience be discussed in terms of (a) specific binding between two macromolecules; (b) non-specific charge interactions and (c) steric exclusion (1). The contributions of the different types of interaction are often difficult to separate from each other.

Specific binding can be defined as the binding between two structures which recognize each other in the same way as an enzyme recognizes its substrate or an antibody its antigen. There may be several forces which cause the binding e.g. electrostatic, hydrophobic or hydrogen bonds etc. This type of interaction is thus characterized by specificity rather than the mode of binding. It is well-known from the lectin-field. A few specific interactions in which connective tissue polysaccharides are involved have recently gained attention.

The binding between hyaluronate, the globular part of the cartilage proteoglycan and the specific link-protein has all the characteristics of a specific binding (2,3). It involves a decasaccharide-stretch of the hyaluronate. Other polyelectrolytes do not seem to compete for the binding site on the protein. The bond is stable at high ionic strength but can be split by a protein-denaturing agent, guanidine hydrochloride.

Investigations during recent years have shown that most connective tissue polysaccharides are heterogeneous due to chemical modifications of the original polymerization product. Heparin contains for example a large number of different disaccharide structures without any apparent regularity in their sequence. Heparin acts as an anticoagulant by binding to antithrombin (4). This binding is specific and apparently possible only if six disaccharides form a correct sequence. The activity of heparin can therefore be related to the probability that this sequence is present in the molecule. This probability increases with increasing degree of polymerization which explains the molecular weight dependence of the anticoagulant activity of heparin (5).

Charge interaction. The negatively charged polysaccharides may bind positively charged macromolecules, mostly proteins. This binding is often non-specific. The binding is sensitive to pH and ionic strength and is a function of a number of variables such as the charge densities on the molecules, the nature of the charged groups etc (6). The electrostatic interaction has been studied by numerous techniques and utilized for various practical purposes. It has been demonstrated that it can induce conformational changes in proteins (7). The electrostatic interactions which are of physiological interest are, however, those which are formed in solution at physiological pH and ionic composition. Only a few systems studied have been biologically relevant such as the interactions between connective tissue polysaccharides and collagen (8) and lipoproteins (9) respectively.

Steric exclusion. Two or more molecules cannot occupy the same position at the same time and they therefore mutually exclude each other from the domains that they occupy. Asymmetric molecules such as linear polysaccharides exert a larger exclusion effect on other macromolecules than compact molecules do. Exclusion is an entropic interaction, i.e. it does not directly produce any heat effect between interacting components. Exclusion of a compound in solution can be registered as an increase in its activity coefficient (10,11).

Steric exclusion has been demonstrated by many different methods and the magnitude of the effect of connective tissue polysaccharides on plasma proteins is now well established. In vitro results have recently been confirmed by in vivo studies on the exclusion from connective tissue compartments (12). The steric interaction can influence such properties as the solubility and conformation of macromolecules and equilibria in chemical reactions.

Various aspects of the physiology of connective tissue will be discussed on the basis of the physical chemical properties of the proteoglycans and their interactions with other macromolecules (13).

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