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The CH-Surface Area of Sugar Molecules as a Measure of Their Potential Hydrophobicity

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Synopsis. Differential affinity of three groups of sugars (monosaccharides, glucodisaccharides and methyl glycosides) can reasonably be interpreted in terms of a molecular surface parameter, the ratio of the surface area of hydrophobic groups (CH, CH_2, and CH_3) to that of hydrophilic groups (OH and -O-) computed from the crystallographic data.

We reported several items of evidence indicating the potential hydrophobicity of sugars:[1–5] these include the configuration- and conformation-dependent affinity of sugars for polystyrene gel in aqueous solvents, which is also strongly affected by the type of salt (chaotropic or nonchaotropic) present, the cosolvent effect of sugars increasing the aqueous solubilities of hydrocarbons and 1-alkanols, and the strong affinity of *n*-aliphatic alcohols for dextran gel. In these studies, the hydrophobicity of sugars was measured in terms of their partition coefficients (K_{av}) between polystyrene gel (Bio-Beads SM-4, Bio-Rad Labs) and aqueous solvent. Inspection of the K_{av} spectrum of various sugars including monosaccharides, deoxy sugars, methyl glycosides and oligosaccharides led us to conclude that the hydrophobic behaviors of sugars are due to CH, CH_2, and CH_3 groups of the sugar molecules. Indeed, for monosaccharides, Miyajima et al.[6] showed that the polystyrene affinity ($\ln K_{av}$) is closely correlated with a CH-surface parameter, index A which is defined as the percent ratio of the total surface area of the hydrophobic groups (CH and CH_2) to that of the hydrophilic groups (OH and -O-). However, the CH index,[5] a CH-surface parameter defined on essentially the same basis as index A, totally fails to predict the order of the polystyrene affinity of glucodisaccharides and methyl glycosides where the effect of other molecular properties such as molecular planarity, rigidity and spatial segregation between OCH_3 and OH groups may become important.[5] Nevertheless, since the CH-surface effect seems to be the primary factor giving rise to the hydrophobic behaviors of sugars, it is of interest and profitable to examine the correlation between the polystyrene affinity and the CH index over a wide range of K_{av}.

The surface area is defined by the area of the surface traced out by the center of spherical water molecule of radius 1.4 Å sliding over the surface of sugar molecule.[7] The orthogonal atomic coordinates of sugar molecules were obtained from the Cambridge crystallographic data file (CAM), and the surface area was calculated using the computer program ASA written by H. Mizuno (Kyushu Univ.). The CH index was defined by

$$\text{CH Index} = \frac{\text{Total surface area of CH, CH}_2\text{, and CH}_3\text{ groups}}{\text{Total surface area of OH, and -O- groups}}$$

which is formally identical to the Index A of Miyajima et al.[6] but differs in that, instead of assuming the free rotations of OH groups about the C–O linkages, the crystallographic atomic coordinates were used to calculate the surface area and that the parameters accounting for the 2α- and β- anomer equilibrium of glucodisaccharides were dropped out. Accordingly, the CH indexes of glucodisaccharides (Fig. 1) are those of β-anomers. The chromatographic partition coefficients (K_{av}) of sugars, obtained using a column of polystyrene beads (Bio-Beads SM-4) in 2 mol dm^{-3} NaCl,[2,5] can be correlated with the association constant (K) for sugar-polystyrene interaction by

$$K = \frac{1}{[\mathrm{B_o}]}\left(\frac{K_{av} - K^{o}_{av}}{K^{o}_{av}}\right)$$

where $[\mathrm{B_o}]$ is the total concentration of the independent and equivalent binding sites in the volume of the polystyrene gel phase accessible to sugar molecules,

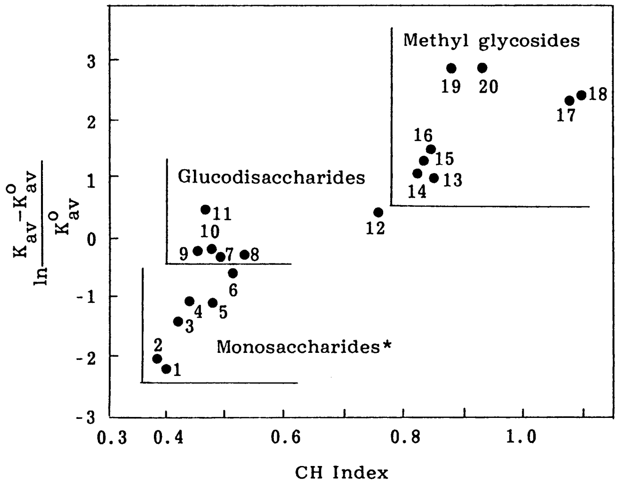

Fig. 1. Correlation between the polystyrene affinity and CH index. CH index=ratio of total surface area of CH, CH_2, and CH_3 groups to total surface area of OH and O groups. 1: galactose, 2: glucose, 3: mannose, 4: xylose, 5: arabinose, 6: ribose, 7: cellobiose, 8: maltose, 9: trehalose, 10: gentiobiose, 11: laminaribiose, 12: deoxyribose, 13: β-methyl D-galactoside, 14: α-methyl D-galactoside, 15: β-methyl D-glucoside, 16: α-methyl D-glucoside, 17: β-methyl D-xyloside, 18: β-methyl D-arabinoside, 19: α-methyl D-mannoside, 20: α-methyl D-xyloside. *: Data of CH-surface area from Miyajima et al. (Ref. 6).

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and K°_{av} is the partition coefficient in the absence of sugar-polystyrene interactions.[2] Accordingly, $\ln[(K_{av}-K^{\circ}_{av})/K^{\circ}_{av}]$ is a measure of the standard free energy of sugar-polystyrene interaction and hence it was taken as a measure of the polystyrene affinity of sugars in the present study.

Figure 1 shows the polystyrene affinity, $\ln[(K_{av}-K^{\circ}_{av})/K^{\circ}_{av}]$, of monosaccharides, glucodisaccharides and methyl glycosides plotted against the CH index. As previously noted,[5] the parallelism between the order of the polystyrene affinity and that of the CH index does not hold for glucodisaccharides and methyl glycosides. However, it is important to note that on the macroscale the CH index well correlates with the polystyrene affinity of sugars. Strictly, direct comparison of monosaccharides (methyl glycosides included) with disaccharides may not be valid as the multi-point interactions of sugar molecule with polystyrene will increase with increase of the molecular weight of sugars. (Note that the effect of the multi-point interactions, in which the hydrophobic surfaces on the glucose residues of the disaccharide molecules contribute cooperatively, but not additively, to the polystyrene affinity, is not taken into account in the formulation of K nor of the CH index.) Indeed, for monosaccharides and methyl glycosides an approximate linearity appears to exist between the two parameters. This strongly suggests that the hydrophobicity of sugars is primarily determined by the hydrophobic/hydrophilic surface balance. The failure of the CH index to predict the order of K_{av} of α and β-methyl D-mannosides ($\alpha(10.6) \gg \beta(4.3)$) indicates that the neglect of the anomeric equilibrium effect in the calculation of the CH index does not impose a serious limitaion on the validity of the CH index. Rather, more or less poor accuracy of the CH index compared with index A may be attributed to an increase in the conformational freedom of glucodisaccharides and methyl glycosides leading to an increased deviation from the crystalline state.

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