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Sweet–bitter interactions and the solution properties of chlorinated sugars

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Abstract

Among chlorinated sugars, some are intensely sweet, some are bitter and others are tasteless. Although chlorination of sugars provokes an increase in lipophilicity, a certain hydrophilic/lipophilic balance is needed for sweeteners to be perceived. Two chlorinated sugars, sucralose (trichlorogalactosucrose) and methyldichlorogalactoside, respectively known for their enhanced sweetness (650×) and inhibitory effect on the sweetness of sucrose, are studied. Their sapid properties are interpreted on the basis of their physicochemical properties (intrinsic viscosity, apparent specific volume, surface tension, contact angle and vibrational spectra). It is particularly shown that the perturbation of the structure of water by these molecules, compared with that by simple sugars, helps in understanding their taste mechanism. © 1998 Elsevier Science Ltd. All rights reserved.

1. Introduction

The discovery by Hough and Khan (1989) of the enhanced sweetness of the chlorodeoxy-derivatives of sucrose raised the problem of the explanation of the enhancement of sweetness after chlorinating. Wiet and Miller (1997) have recently suggested that chlorine substitution is merely enhancing the intrinsic sensory qualities of sucrose. Other chemical modifications of sugars such as methylation, ethylation, propylation, butylation or benzylation generally lead to bitter derivatives. Depending on the position of the chloro-substituent and on the resulting hydrophilic/lipophilic balance of the molecule, the derivatives of sucrose may be found to be intensely sweet, sweet, bitter–sweet or even bitter. On the other hand, derivatives of galactosucrose are all intensely sweet; the positions for sweetness enhancement by chlorine substitution being $4,1',4'$ and $6'$. These positions are mainly opposite to the hydrophilic moiety which is attributed to the AH-B system (see Fig. 1). The increase in lipophilicity after chlorinating proves to be one of the clues to enhanced sweetness (Van der Heijden, 1993).

Sweetness and bitterness are found to interact and compensate each other. In the same molecule, the intrinsic bitterness of the bitter end may depress the sweetness of the molecule (Birch and Lee, 1976). Mixing solutions of quinine sulfate and sucrose causes a depression of the subjective intensity of sweetness and a depression of bitterness. In a recent holistic approach (Shallenberger, 1993), sweetness and bitterness were linked to the symmetric or dissymmetric character of the sapophore.

The hydrophobic character of sapid molecules seems important in sweet taste perception. According to Daniel (1989), the hydrophobicity of the stimulus affects its accession and its distribution onto the receptor. Several methods of hydrophobicity evaluation have been published. Janado and Yano (1985) determined the nature of sugars by their differential affinity for polystyrene gel in aqueous solvent (partition coefficient K_{av}). Iwase et al. (1985) determined the partition coefficient defined by Leo et al. (1971) using the calculated solvent accessible surfaces areas. Miyajima et al. (1985) characterized several monosaccharides by their hydrophobic index (A and B) expressed as the ratio (hydrophilic area/hydrophobic area). According to Yano et al. (1988), the lipophilicity of sugars probably results from an equilibrium between these two estimated areas.

In this work, we determine the lipophilicity of sugars (sucrose, D-fructose, D-glucose), intense sweetener (sucralose), sweetness inhibitor (α-methyl 4,6 dichloro-

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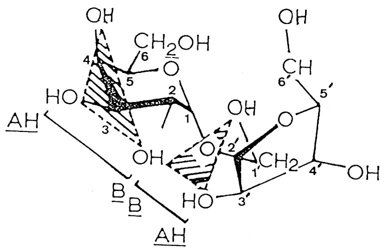

substitution		Atom / position					taste
		4	6	1'	4'	6'	
(a) sucrose	mono	-	-	Cl	-	-	20
		-	Cl	-	-	-	Bitter
		-	-	-	-	Cl	20
	di	-	-	Cl	Cl	-	30
		-	-	Cl	-	Cl	76
		-	Cl	-	-	Cl	Not sweet
	tri	-	-	Cl	Cl	Cl	100
	tetra	Cl	Cl	Cl	-	Cl	100
(b) galacto-sucrose	mono	Cl	-	-	-	-	5
	di	Cl	-	Cl	-	-	120
	tri	Cl	-	-	Cl	Cl	160
		Cl	-	Cl	Cl	-	220
		Cl	-	Cl	-	Cl	650
	tetra	Cl	Cl	Cl	-	Cl	200
		Cl	-	Br	Br	Br	30
		F	-	Cl	Cl	Cl	200
		Cl	-	Cl	F	Cl	1000
		Cl	-	Cl	Cl	Cl	2000
		Cl	-	Cl	Br	Cl	3000
		Cl	-	Cl	I	Cl	7000
		Br	-	Br	Br	Br	7500

(van der Heijden, 1993)

Fig. 1. Derivatives of galactosucrose.

4,6-dideoxy-D-galactopyranoside) and a bitter compound (quinine sulfate) from their interfacial properties by measuring the contact angle formed between a hydrophobic surface and the aqueous solution of the studied compounds. Adhesion force of the studied solutions on such holders is calculated from surface tension and contact angle measurements. The affinity of the studied compounds for a hydrophobic support can be related to their spreading over the proteinaceous receptor membrane. We also determine the hydration properties (intrinsic viscosity, Huggins coefficient, apparent specific volume and hydration number) of the studied molecules in aqueous solutions as well as their Ftir and Raman spectra. Comparison of physicochemical properties of sweet, bitter and sweetness inhibitor compounds helps in elucidating the role of water in the quality of taste.

2. Materials and methods

Sucrose, D-glucose and D-fructose are Sigma products, all with a purity >99%. Quinine sulfate is a Prolabo product. The synthesis of α-methyl 4,6 dichloro-4,6-dideoxy-D-galactopyranoside (methyl dicl-gal) was carried out using the procedures of Bragg *et al.* (1959), Jones et al. (1960) and Jennings and Jones (1962, 1963, 1965). Trichlorogalactosucrose TGS (sucralose) was donated by Prof. Plusquellec (E.N.S.C., Rennes, France).

2.1. Intrinsic viscosity [η]

Intrinsic velocity is determined using a semi-automatic Schott AVs 400 viscometer by measuring the time for a given volume to flow through a capillary at a constant temperature of 25±0·02°C. A triple extrapolation procedure was applied for accurate determination of [η] (Mathlouthi et al., 1993a). The equation of Huggins (1942) was used to determine the interaction parameter, Huggins constant k'. Apparent specific volumes ASV ($V_2°$) were calculated from density measurements at 25±0·1°C determined with a PAAR densitometer (DMA 45). Estimation of the hydration number h was done according to Herkovitz and Kelley (1973).

2.2. Surface tension (γ)

Surface tension was obtained with a semi-automatic D2000 (Prolabo) tensiometer using a platinum blade wrench method at 25±0·1°C. Slightly mineralised buffered water ('Volvic') was used for preparation of solutions.

2.3. Contact angle (θ)

Contact angle measurements were made with a goniometer (type G40, KRÜSS) and consisted in determining the affinity of a sweetener solution for a hydrophobic surface (polyethylene). A drop of sweetener solution was introduced on a sheet of polyethylene with a syringe; a micro-camera connected to a computer allows calculation of θ values from the position of the droplet on the support.

2.4. Fourier-transform infrared (FTIR) and Laser Raman spectra

These were recorded according to methods previously described (Mathlouthi and Seuvre, 1988). Concentrations used for all measurements were 10% (w/v) sugar and 1% (w/v) TGS, bitter and inhibitor substance.

3. Results and discussion

3.1. Solution properties

As already reported (Mathlouthi et al., 1993a), sweet taste chemoreception may be based on the interpretation of sweetener solution properties. Intrinsic viscosity [η] and Huggins constant k' results are listed in Table 1 for sugars, α-methyl 4,6 dichloro-4,6-dideoxy-D-galactopyranoside (methyl dicl-gal) and trichlorogalacto

Table 1
Viscometric and volumetric properties for 10% (w/w) sugar, 1% (w/w) TGS, 1% (w/w) methyl-dichlorogalactose and 0·1% (w/w) quinine sulfate at 25°C

	$[\eta]$ ($cm^3\,g^{-1}$)	k'	ASV ($cm^3\,g^{-1}$)	h
Sucrose	2.37	1.15	0.62	6.14
D-fructose	2.37	1.14	0.62	3.26
D-glucose	2.29	0.89	0.61	3.01
TGS	1.8	2.12	0.60	—
Methyl-dicl-gal	2.71	1.12	0.66	5.50
Quinine sulfate	—	—	0.75	—

sucrose (TGS). As may be observed, the lowest $[\eta]$ and the highest k' values are found for TGS because of the marked difference between its hydrophobic and hydrophilic sides and its higher flexibility around the glycosidic linkage. On the other hand, the highest $[\eta]$ value is found for α-methyl 4,6 dichloro-4,6-dideoxy-D-galactopyranoside (Table 1), probably on account of the hydrophobic effect of chlorine and methyl substituents which immobilizes water molecules around the solute.

Apparent specific volume was found to be the most valuable parameter to discriminate the four basic tastes (Shamil et al., 1987). Sweetness corresponds to ASV values ranging from 0·52 to 0·70 $cm^3\,g^{-1}$ and bitter taste to ASVs from 0·71 to 0·93 $cm^3\,g^{-1}$. Table 1 shows that the values of ASV for sugars and TGS are situated in the middle of the range of ASVs for sweet taste whereas methyl dicl-gal and quinine sulfate have an ASV value in the range for bitter taste.

3.2. *Interfacial properties*

Surface tension (γ) which accounts for the modifications of water cohesiveness by solutes, is measured for 10% (w/w) sugar, 1% (w/w) TGS and 1% (w/w) methyl dicl-gal and 0·1% (w/w) quinine sulfate. Results are given in Table 2. As may be observed from γ values, sugars do not seem to affect the cohesion of water molecules at macroscopic level because of their overall hydrophilic character. On the other hand, TGS, quinine sulfate and, in a more pronounced manner, methyl dicl-gal provoke a rapid decrease in surface tension of water from 73·7 to 52·6 mN m^{-1} after addition of only 1% methyl dicl-gal. This detergent effect is related to the relatively high concentration of solute at the water/air interface, due to the orientation of lipophilic groups towards the surface of the solution.

Table 2
Surface tension γ (mN m^{-1}), contact angle θ (°) and adhesion force W_{ls} (mN m^{-1}) for 10% (w/w) sugar, 1% (w/w) TGS, 1% (w/w) methyl-dichlorogalactose and 0·1% (w/w) quinine sulfate in water at 20°C

Compound	γ (mN m^{-1})	θ (°)	W_{ls} (mN m^{-1})
Sucrose	74.0	96.3	65.8
D-fructose	74.3	95.9	66.6
D-glucose	74.0	99.4	61.8
TGS	66.3	82.6	74.8
Methyl dicl-gal	52.6	83.6	58.4
Quinine sulfate	67	90.7	66.2

Contact angle (θ) measurements were carried out on solutions of sugars (sucrose, D-glucose and D-fructose), TGS, methyl dicl-gal and quinine sulfate. Results are listed in Table 2. Sugars are characterized by values lying between 99·4 and 95·9° while the other compounds show lower values (90·7 to 82·6°). These results indicate that the intense sweetener TGS, quinine sulfate and the inhibitor (methyl diclgal) show a better fit with the hydrophobic surface and can be distinguished from sugars by a relatively marked lipophilic character.

Adhesion force (W_{ls}) at the liquid/solid interface is calculated from contact angle and surface tension by use of the Dupré-Young relation: $W_{ls} = \gamma\ (1 + \cos\ \theta)$. Results in Table 2 show higher W_{ls} values for the intense sweetener, TGS, and lower values for the sweetness inhibitor, methyl dicl-gal, than for sugars. The value obtained for the bitter compound, quinine sulfate, is comparable to that of sugars. This parameter expresses the affinity of the solution for a hydrophobic surface while accounting for the concentration of solutes at the water/air interface. A correlation was recently (Hutteau and Mathlouthi, 1998) found between W_{ls} and relative sweetness, showing that the higher the sweetness intensity, the larger the value of W_{ls}.

The studied solution properties are only informative about the general behaviour of sapid molecules in aqueous solutions. They allow a clear differentiation of the sweet molecules from the bitter or inhibitor ones, which in turn suggests that the accession to site entails an optimal specific volume. The intense sweetener TGS, because of the marked difference between its hydrophilic and hydrophobic ends and its flexibility around the glycosidic bond (Mathlouthi and Seuvre, 1988), provokes an increase in mobility of water manifested by a low $[\eta]$ and high k'. From interfacial properties, TGS, quinine sulfate and especially methyl dicl-gal exhibit a high detergent effect. These compounds also show a certain lipophilic character. Since increased hydrophobicity is related to bitterness, methyl dicl-gal, because of its tensio-active behaviour, probably acts as a bitter substance which inhibits the sweetness of sucrose by masking the site of reception of the sweet taste.

3.3. *Vibrational spectroscopy*

3.3.1. *Fourier transform infrared (Ftir)*

Ftir spectra of β-D-fructopyranose, α-D-glucopyranose, sucrose, methyl dichloro-galactoside and TGS in

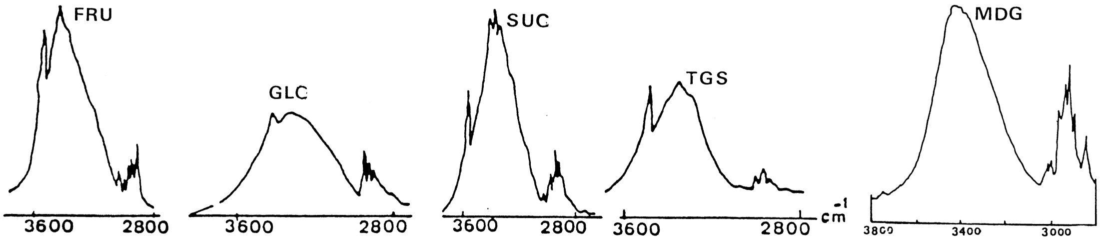

Fig. 2. Ftir spectra of D-Fructose (FRU), D-Glucose (GLC), sucrose (SUC), trichlorogalactosucrose (TGS) and methyl-dichlorogalactoside (MDG) in the region of OH streching.

the 2700–3700 cm^{-1} range are illustrated in Fig. 2. A sharp absorption between 3500 and 3600 cm^{-1} is observed for D-fructose, sucrose and TGS. D-glucose shows only a shoulder. This absorption is generally assigned to free OH vibration (O...O > 3 Å). Such a hydroxyl group, which does not take part in the hydrogen bonding in the crystal, was found to characterize the sweetest sugars. The taste inhibitor, methyl dicl-gal, did not show any free OH in its spectrum. Indeed OHs in the crystal are involved in inter-residue H-bonding (Mathlouthi et al., 1993b): O_2–H donates a hydrogen bond to the O_3 atom of a neighbouring molecule and O_3–H is implicated symmetrically in bifurcated hydrogen bonds to O_1 and O_2. The hydrogen bonding in this chlorinated derivative is essentially two dimensional and situated in sheets parallel to the *ab* plane separated by sheets which only contain the hydrophobic methyl and chloromethylene groups.

The interpretation of Ftir spectra helps in defining the tripartite glucophores. The sharpest band is generally assigned to the donor AH in the couple AH-B. If no individualized band is observed, more than one glucophore is possible and the sweetness intensity is lowered (Mathlouthi and Portmann, 1990).

In order to verify the possible existence of a direct weak interaction between sucrose and the inhibitor of its sweetness, the spectra of their mixture (sucrose+-methyl dicl-gal) were studied (Mathlouthi et al., 1993b). The i.r. spectrum of sucrose was found to show an individualized peak at 3550 cm^{-1}and that of the mixture did not anymore show a shoulder. This modification of the sucrose spectrum was assigned to the modification of the aqueous environment by the addition of the hydrophobic chloro-derivative.

3.3.2. *Raman spectroscopy*

Raman spectroscopy is generally better suited for the study of the effect of the lipophilicity of chlorinated sugars on water structure. We use it as a comparative method of study. The spectrum of pure water was first decomposed into four components according to the method of Luu and coworkers (1982) (see Fig. 3 and Table 3). Frequencies and intensities of the four components were determined. Using the same program of decomposition of the experimental Raman band, we determined the four components (a, b, c and d) of OH band spectra for water in the presence of solutes.

The shifts in frequencies and variations of integrated intensities (peak area) provoked by the addition of sugars and their chloro-derivatives to water are presented in Table 4.

Small carbohydrates, as expected, do not cause any noticeable change in water structure. Only small shifts in frequencies are generally caused by 10% of sugars which have an overall structure-maker effect. On the other hand, the chloro-derivatives of sucrose act on water molecule associates. For TGS, frequencies were shifted towards lower values which is a sign of reinforced hydrogen bonds in water. This may be attributable to the increased lipophilicity of TGS. The

Table 3
Position of maximum (υ), integrated intensity (area %), shifts in frequencies (Δυ) and of area (Δ area %) of the Raman band of pure water

Component	v (cm^{-1})	Area (%)	Assignment
a	3239	64.1	Quasi-crystalline phase
b	3414	20.8	Solid-like amorphous phase
c	3537	13.5	Liquid amorphous phase
d	3633	1.7	Unassociated H_2O molecules

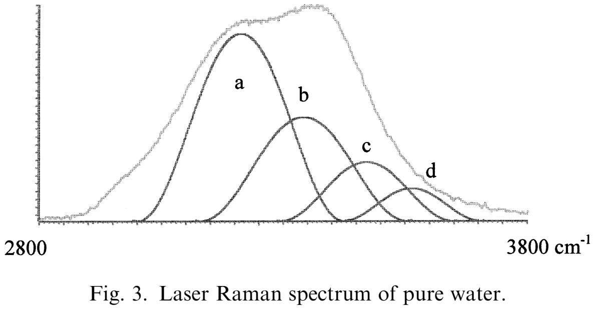

Fig. 3. Laser Raman spectrum of pure water.

Table 4
Position of maximum (υ), integrated intensity (area %), shifts in frequencies ($\Delta\upsilon$) and of area (Δ area %) of the Raman band of water, sugars, methyl diclgal and TGS

Component	υ (cm^{-1})	Area (%)
Water		
a	3239	64.1
b	3414	20.8
c	3537	13.5
d	3633	1.7

Component	$\Delta\upsilon$ (cm^{-1})	Δ Area (%)
Glucose		
a	5	0
b	4	1
c	−3	−1
d	0	0
Fructose		
a	6	0
b	4	0
c	0	−1
d	0	0
Sucrose		
a	6	0
b	3	−1
c	−3	0
d	−2	0
Methyl dicl-gal		
a	5	−1
b	17	5
c	24	−5
d	8	0
TGS		
a	−12	−14
b	−6	13
c	−8	−3
d	−11	4

integrated intensities show a decrease in the weight of the quasi-crystalline water and an increase in the proportions of the less organised species. Thus, the global effect of TGS is quantitatively an increase of mobility of water structure although the amorphous species are more tightly linked.

For 0·1% methyl dicl-gal, important shifts in frequencies towards higher values are observed (Table 4). The overall effect of methyl dicl-gal is the reverse of what was observed with TGS. The perturbation of water structure by this bitter compound is manifested by higher shifts in frequencies for the four components (+5 to +24 cm^{-1}) and an increase in intensity of component b (+6%) (whereas that of TGS is decreased).

In order to interpret the inhibition of sucrose sweetness by methyl dicl-gal, the Raman spectrum of the mixture (10% sucrose +0·2% inhibitor) was recorded in the region 3800–2800 cm^{-1} and the experimental band decomposed and compared with that of pure water. The calculated frequencies and intensities and their comparison with that of water showed a preponderant effect of methyl dicl-gal. While sucrose only slightly modified the structure of water (frequencies showed a maximum shift of 6 cm^{-1} for component a), the preponderance of the effect of methyl dicl-gal was manifested by shifts in frequencies of up to 34 cm^{-1} for component c and −11 cm^{-1} for component a (Table 5). The perturbation of the four species of water associates, more important than with sucrose alone, was appreciable with a very small amount of methyl dicl-gal (0·2%). When the chlorinated galactose is tasted it might bind to the receptor and prevent the access of sucrose molecules to the site. As it binds via its pair of OHs (O_2-H and O_3-H) there is no remaining hydrophilic character and all the rest of the molecule is hydrophobic. The consequence is the repulsing of water molecules which then associate in clathrate like clusters. Their mobility is hindered and the ionic exchange across the membrane is impeded, so no sweet sensation is perceived.

Table 5
Position of maximum (υ), integrated intensity (area %), shifts in frequencies ($\Delta\upsilon$) and of area (Δ area %) of the Raman band of water and the mixture (10% sugar +0·2% methyl dicl-gal)

Component	υ (cm^{-1})	Area (%)	$\Delta\upsilon$ (cm^{-1})	Δ Area (%)
a	3239	64.1	−11	−10
b	3414	20.8	12	18
c	3537	13.5	34	−8
d	3633	1.7	3	0

An alternative argument, from the effect of methyl dicl-gal on water structure, is that the inhibition effect is not competitive. It could be due to the hydrophobic effect of the galactoside. When this inhibitor is in solution (saliva), the molecules can associate pairwise through intermolecular H-bonding. The whole surface surrounding the dimers is hydrophobic and this provokes an important decrease in water mobility. These dimers do not establish any direct interactions with the receptor but they do cause a steric hindrance. This steric hindrance, together with the effect on water structure, is at the origin of the inhibitory action of methyldichlorogalactoside on the taste of sucrose.

Oppositely, the enhanced sweetness of TGS is due to increased mobility of water in the aqueous solution of TGS. The hydrophobic end of the molecule is well equilibrated with the hydrophilic side. The hydrophobicity of the chloromethylene groups contributes to reinforce the hydrogen bonds that the C_2 and C_3 OHs on the fructosyl moiety can establish with the receptor site. Rather than a tripartite (AH-B,γ) glucophore, the molecule of TGS possesses a well equilibrated hydrophilic/lipophilic balance which may be at the origin of its enhanced sweetness.

4. Conclusion

Interpretation of the inhibitory effect of α-methyl 4,6 dichloro-4,6-dideoxy-D-galactopyranoside or the enhanced sweetness of trichlorogalactosucose (sucralose) is based on their solution properties and the vibrational spectra of their solutions. The physicochemical properties show that the substitution in the molecule of OH by chlorine group induces a relative increase in lipophilicity. This implies, for TGS, an increase in water mobility and then a decrease in intrinsic viscosity, apparent specific volume and surface properties. Contact angle measurements seem to be good discriminants for estimating hydrophobicity of solutes. Among sugars, fructose is differentiated by a slightly elevated hydrophobicity. Methyl dicl-gal, quinine sulfate and TGS seem to be characterized by a pronounced hydrophobicity and a detergent effect (especially methyl dicl-gal). The sweetness inhibitory effect of methyl dicl-gal can be attributed to its tensioactive properties and its bitter taste.

At a microscopic level, the Ftir spectra of TGS and methyl dicl-gal are differentiated by an individualized sharp OH band, obtained for TGS, which seems to correspond to its increased sweetness. Analysis of Raman spectra shows opposed effects for TGS and α-methyl 4,6 dichloro-4,6-dideoxy-D-galactopyranoside on water structure. Our physicochemical approach, which consists in determining the perturbation of water structure by sucrose chloro-derivatives, both at macroscopic and microscopic levels, emphasizes the predominant role of water in sapid interactions and helps in interpreting the mechanism of sweetness chemoreception.

References

Birch, G. G. and Lee, C. K. (1976) Structural functions and taste in the sugars series: the structural basis of bitterness in sugars analogues. *J. Food Sci.* **41**(1), 1403–1407.

Bragg, P. D., Jones, J. K. N. and Turner, J. C. (1959) The reaction of the sulfuryl chloride with glycosides and sugar alcohols. Part I. *Can. J. Chem.* **37**, 1412–1416.

Daniel, J. R. (1989) Sweetness: theory and design. In *Frontiers in Carbohydrate Research*–1, eds. R. P. Millane, J. N. Be Miller and R. Chandrasekaran. pp. 34–65. Elsevier Applied Science, London.

Herkovitz, T. T. and Kelley, M. (1973) Viscosities studies of aqueous solutions of alcohols, ureas and amides. *J. Phys. Chem.* **77**, 381–388.

Hough, L. and Khan, R. (1989) Enhancement of the sweetness of sucrose by conversion into chloro-deoxy-derivatives. In *Progress in Sweeteners,* ed. T. H. Grenby. pp. 97–120. Elsevier Applied Science, London.

Huggins, M. L. (1942) The viscosity of dilute solutions of long chain molecules. IV. Dependence on concentration. *J. Am. Chem. Soc.* **64**, 2716–2718.

Hutteau, F. and Mathlouthi M. (1998) Physicochemical properties of sweeteners in artificial saliva and determination of a hydrophobicity scale for some sweeteners. *Food Chem.* **63**(2), 199–206.

Iwase, K., Komatsu, K., Hirono, S., Nakagawa, S. and Moriguchi, I. (1985) Estimation of hydrophobicity based on the solvent-accessible surface area of molecules. *Chem. Pharm. Bull.* **33**, 2114–2121.

Janado, M. and Yano, Y. (1985) Hydrophobic nature of sugars as evidenced by their differential affinity for polystyrene gel in aqueous media. *J. Sol. Chem.* **14**(12), 891–902.

Jennings, H. J. and Jones, J. K. N. (1962) The reaction of sulfuryl chloride with reducing sugars: Part I. *Can. J. Chem.* **40**, 1408–1414.

Jennings, H. J. and Jones, J. K. N. (1963) The reaction of chlorosulfate esters of sugars with pyridine. *Can. J. Chem.* **41**, 1151–1159.

Jennings, H. J. and Jones, J. K. N. (1965) The reaction of sugar chlorosulfates. Part II: The synthesis of chlorodeoxysugars. *Can. J. Chem.* **43**, 2372–2386.

Jones, J. K. N., Perry, M. B. and Turner, J. C. (1960) The reaction of the sulfuryl chloride with glycosides and sugar alcohols. Part II. *Can. J. Chem.* **38**, 1122–1124.

Leo, A., Hansch, C. and Elkins, D. (1971) Partition coefficients and their uses. *Chem. Rev.* **71**(6), 525–555.

Luu, C., Luu, D. V., Rull, F. and Sopron, F. (1982) Raman effect study on structural perturbation of liquid water by foreign substance. *J. Mol. Struct.* **81**, 1–10.

Mathlouthi, M. and Portmann, M. O. (1990) Hydrogen bonding and the sweet taste mechanism. *J. Mol. Struct.* **237**, 327–338.

Mathlouthi, M. and Seuvre, A. M. (1988) Solution properties and the sweet taste of small carbohydrates. *J. Chem. Soc., Faraday. Trans.I.* **84**, 2641–2650.

Mathlouthi, M., Bressan, C., Portmann, M. O. and Serghat, S. (1993a) Role of water structure in sweet taste chemoreception. In *Sweet Taste Chemoreception*, eds. M. Mathlouthi, J. A. Kanters and G. G. Birch. pp. 141–174. Elsevier Applied Science, London.

Mathlouthi, M., Maciejewski, C., Serghat, S., Hoof, R. W. W., Kanters, J. A. and Kroon, J. (1993b) Structural studies on sweet taste inhibitors: methyl-4,6-dichloro-4,6-dideoxygalactopyranoside. *J. Mol. Struct.* **291**, 173–183.

Miyajima, K., Machida, K. and Nakagaki, M. (1985) Hydrophobic indexes for various monosaccharides. *Chem. Soc. Jap.* **58**, 2595–2599.

Shallenberger, R. S. (1993) Chemical aspect of the glucophore/glycophore. In *Sweet Taste Chemoreception*. eds. M. Mathlouthi, J. A. Kanters and G.G. Birch. pp. 75–90. Elsevier Applied Science, London.

Shamil, S., Birch, G. G., Mathlouthi, M. and Clifford, M. N. (1987) Apparent molar volumes and tastes of molecules with more than one sapophore. *Chem. Senses* **12**(2), 391–409.

Van der Heijden (1993) Structure of sweeteners: an overview. In *Sweet taste Chemoreception*, eds M. Mathlouthi, J. A. Kanters and G. G. Birch, pp. 103–127. Elsevier Applied Science, London.

Wiet, S. G. and Miller, G. A. (1997) Does chemical modification of tastants merely enhance their intrinsic taste qualities?. *Food Chem.* **58**(4), 305–311.

Yano, Y., Tanaka, K., Doi, Y. and Janado, M. (1988) The CH-surface area of sugar molecules as a measure of their potential hydrophobicity. *Chem. Soc. Jap.* **61**, 2963–2964.