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Food Chemistry 71 (2000) 309–317

Food Chemistry

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An empirical model to predict the headspace concentration of volatile compounds above solutions containing sucrose

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Received 4 January 2000; received in revised form 20 May 2000; accepted 31 May 2000

Abstract

An empirical model was developed to describe and predict the change in gas–liquid partition behaviour of a wide range of volatile compounds in aqueous sucrose solutions. The static equilibrium headspace concentrations of 40 volatiles (from different chemical classes e.g. pyrazines, alcohols, esters and ketones and with different physical properties e.g. volatility and solubility), were measured above aqueous sucrose solutions [0–65% (w/v)]. As sugar concentration increased, the headspace concentration of some compounds increased, whilst others stayed the same or decreased. The changes in volatile headspace concentrations were correlated (using partial least squares regression) with a range of physicochemical descriptors which were calculated from the compound structure. The model was composed of seven physicochemical descriptors and had a regression coefficient, $R^2 = 0.74$. An external test set was used to validate the model. The key descriptors in the model were $(\log P)^2$, LUMO energy and a connectivity index term. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

The perception of food flavour occurs when flavour compounds are released from a food matrix and transported through the liquid and gas phases to the flavour receptors in the nose and mouth. Much work has focused on the release of volatile flavour compounds from aqueous systems as this is a major route for flavour release before, and during, eating (Overbosch, Afterof & Haring, 1991; Plug & Haring, 1994; Taylor, 1998, 1999). In beverages, for example, volatile flavour compounds are released into the headspace prior to eating and make their way via the orthonasal route to the olfactory receptors, providing our first impression of the flavour. During drinking, further release occurs in the mouth, although the rate and extent of release will be affected by dilution with saliva, possible changes in temperature and increased surface area. In other food systems, like confectionery, the release mechanisms are more complex. Here, the confectionery matrix dissolves and/or melts to form a sugar rich solution in-mouth (e.g. Hills & Harrison, 1995), from which volatiles are released into the headspace. Release of volatiles from the liquid phase into the gas phase is a dynamic, rather than an equilibrium process during eating. However, in many of these dynamic studies, the gas–liquid partition coefficient has been shown to exert a major effect on the release of volatile compounds (e.g. De Roos & Wolswinkel, 1994; Marin, Baek & Taylor, in press). It is well established that the gas–liquid partition coefficient is affected by the presence of solutes (see for example Voilley, Simatos & Loncin, 1977). The aim of this paper was to develop and test an empirical model based on quantitative structure property relationships (QSPR) so that the headspace concentration of any volatile compound above a sucrose solution could be predicted.

Voilley et al. (1977) studied the change in concentrations of acetone and octanol in the gas phase above aqueous solutions containing sucrose and other solutes. Other workers have determined the change in partition of pentyl acetate above water and sugar solutions (Kieckbusch & King, 1979), the effect of salt, glucose and malic acid on the partitioning of diacetyl between water and air (Land & Reynolds, 1981) and the effect of sugars and artificial sweeteners on orange aroma partition (Nahon, Koren, Roozen & Posthumus, 1998). Solutes can increase, decrease or not affect the headspace concentrations of volatiles. Some authors have described

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PII: S0308-8146(00)00190-4

the general increase of volatile concentration in the headspace when a solute is added to the solution as "salting out" and a decrease as "salting in". Voilley et al. explained this phenomenon in their system by reference to Eq. (1).

$$K^i_{gl} = \left(\frac{\gamma_{\cdot i} P^0_i(T)}{P_T}\right) \cdot \frac{\overline{V}_l}{\overline{V}_g} \quad (1)$$

where K^i_{gl} is the gas–liquid partition coefficient for species i, $\gamma \cdot i$ is the activity coefficient, $P^0_i(T)$ is the vapour pressure for the pure component i (Pa) at temperature T, P_T, the total pressure in the gas phase (Pa) and $\overline{V}_l$, $\overline{V}_g$ are the molar volumes of the liquid and the gas phases respectively (m^3/mol). When a solute is added to the solution, the mole fraction of the liquid phase changes and the activity coefficient can also change. By measuring these parameters for a range of volatiles with different solutes, Voilley et al. rationalised the behaviour of the systems they studied. In brief, an increase in headspace concentration with increasing solute concentration may be due solely to a change in mole fraction (depending on the solute) providing that the activity coefficient remains constant. In other cases, changes in the mol fraction and activity coefficient (with increasing solute concentration) effectively cancel each other out and there is no change in headspace concentration. Decreases in headspace can also be explained by these mechanisms.

The work described above shows the physicochemical nature of the interactions between solutes, like sugar and salt, and volatiles. However, to predict the behaviour of any particular volatile in a solution containing solutes is very time-consuming because it is necessary to determine the activity coefficient for each system as well as calculating the mole fraction for the system in question. In this paper, we study the feasibility of an empirical approach based on QSPR, which has been widely used in other scientific disciplines to relate observed behaviour to physicochemical descriptors. In Environmental Science and Pharmaceutical Science, the release and distribution of pollutants and drugs in biological tissues has been measured experimentally, then modelled using QSPR (Argese, Bettiol, Giurin & Miana, 1999; Lien & Gao, 1995; Sixt, Altschuh & Bruggemann, 1995). The physicochemical descriptors are calculated using software packages like CAChe (Oxford Molecular Ltd., Oxford, UK) or UNIFAC (Reid, Prausnitz & Poling, 1987) so experimental work is limited to measuring the behaviour of the system. Many of the reported uses of QSPR, study molecules with very similar properties whereas flavour chemicals represent a very wide range of physical and chemical properties. However, QSPR has been successfully applied to estimate partition coefficients (Dearden, 1996; Dearden, Cronin, Ahmed & Sharra, 2000; Dearden, Cronin, Sharra, Higgins, Boxall & Watts, 1997; Katritzky, Wang, Sild & Tamm, 1998) and to elucidate the structure-odour relationships of some compounds (Mihara & Masuda, 1988), suggesting that QSPR is applicable to the behaviour of flavour compounds. A QSPR model to describe the release of volatile compounds from gel systems during eating has already been reported from our laboratory (Linforth, Friel & Taylor, in press). This paper describes the application of QSPR to model the effect of sugar solutes on the headspace concentration of volatiles.

2. Materials and methods

2.1. Materials

Volatile compounds (>99% pure) were obtained from Firmenich, (Geneva, Switzerland), Sigma-Aldrich, (Gillingham, UK) or Tastemaker, (Milton Keynes, UK) and were used without further treatment. Sucrose (ACS reagent grade) was obtained from Fisher Scientific UK Ltd., (Loughborough, UK).

2.1.1. Sample preparation

Aqueous sucrose solutions were prepared in a range of concentrations from 0 to 65% (w/v). Volatile compounds were added to these solutions at concentrations below the aqueous solubility limit of each volatile. The volatile concentrations ranged from less than 0.1 mg/kg for compounds such as caryophyllene and terpinolene to 70 mg/kg for ethanol and acetaldehyde. The samples were allowed to equilibrate for 24 h prior to analysis.

2.2. Methods

2.2.1. Headspace analysis by atmospheric pressure chemical ionisation-mass spectrometry (APcI-MS)

Portions of solutions (60 ml) were placed in sealed glass bottles. The headspace (63 ml) above each solution was sampled for approximately 30 s at a flow rate of 15 ml min^{-1} using a heated (100°C) gas phase interface, MS Nose™, into the APcI-MS source (MicroMass, Manchester, UK). There, the volatile compounds were ionised by a 4 kV corona discharge (cone voltage 21 V) before they were sampled into the high vacuum region of the mass spectrometer. This resulted in minimal disturbance to the headspace due to the small volume sampled. A plateau value was rapidly established on the MS chromatogram. The plateau values for three replicates were obtained and converted to headspace concentrations (mg/m^3) using a calibration method (Taylor, Linforth, Harvey & Blake, 2000).

2.2.2. Data processing

The conversion of the raw data (plateau values from traces) to concentrations was carried out using an Excel spreadsheet (Microsoft Corporation, USA). The corre-

lation of sucrose concentration in solution to the headspace concentration of each volatile compound was carried out in Design Expert (v. 5.0.9, Stat Ease Inc., USA) using a linear least squares regression. The regression equations from the linear least squares regression were used to generate the dependent variables to be used in the partial least squares regression, PLS. Partial least squares regression was carried out using the Guideline + multivariate regression software (v. 7.5, CAMO ASA, Norway).

3. Results and discussion

Preliminary experiments were performed to determine the effect of changing the sucrose concentration of an aqueous solution on the headspace concentration of volatiles above the solution. Forty different volatiles were studied at equilibrium in aqueous solutions ranging from 0 to 65% (w/v) sucrose. The traces from the mass spectrometer were converted to headspace concentrations through calibration with authentic standards. However, for the purpose of modelling, the ratios of the headspace concentration above the sucrose solutions and above water, were determined for each compound as this was a convenient parameter and allowed easy comparison of compounds as all values were in the range 0.54–2.46. Increasing the sucrose concentration of the volatile solution produced different headspace concentration ratios (relative effects) which were highly compound dependent (see Fig. 1 for examples). These relative effects, which were initially modelled with linear least squares regression, gave linear models for all of the volatiles over the sucrose concentration range studied (Fig. 1). Using this linear response, an "effect value" was produced for each volatile. The effect value is the ratio of the headspace concentration of the volatile above an aqueous sucrose solution compared to the headspace concentration obtained above water. For the purposes of this paper all results are reported for the maximum sucrose content used [65% (w/v)].

A wide range of effect values was obtained (Table 1) ranging from 0.54 for ethyl decanoate to 2.46 for linalool. This indicates that some volatiles were displaced from the solutions containing high sucrose levels (i.e. linalool) whilst others appeared to be more soluble in it (i.e. ethyl decanoate). Where the presence of sucrose did not change the headspace concentration, an effect value of 1 was assigned (e.g. acetaldehyde).

4. Model development

The effect values were used as dependent variables for regression analysis. A number of different molecular descriptors (independent variables) were generated for each compound using the chemical modelling program CAChe. CAChe uses a number of different methods of generating descriptors, for example, physicochemical descriptors such as log *P*, are generated from an atom typing method (Ghose, Pritchett & Crippen, 1988), whereas for quantum chemical descriptors, such as frontier molecular orbital energies, a molecular mechanics compute engine is used (Stewart, 1990). Sixty individual molecular descriptors were generated and used in regression analysis along with their mathematical relations, e.g. dipole moment, dipole moment squared, reciprocal of dipole moment and log dipole moment etc. (a total of 199 descriptors). These descriptors contained information describing the size, shape

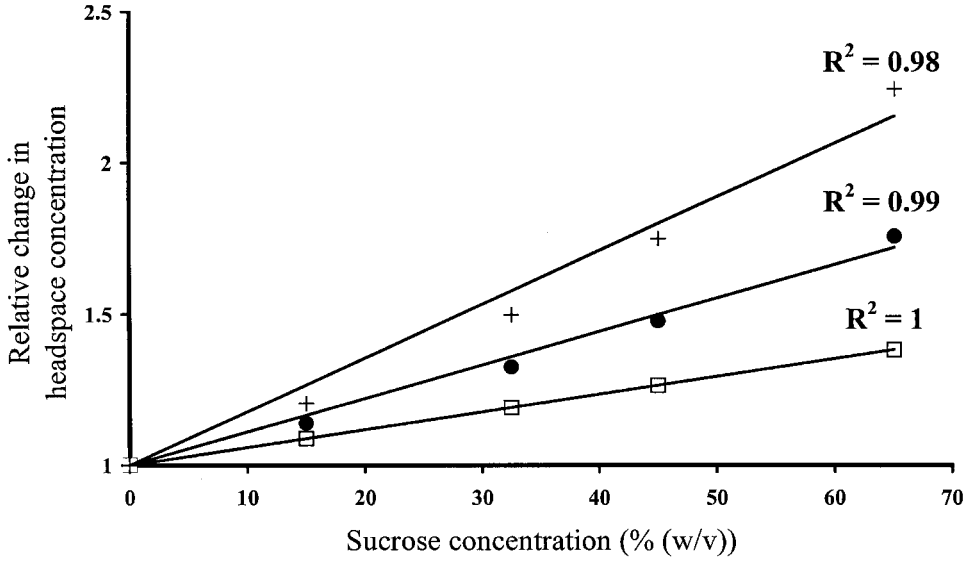

Fig. 1. Relative changes in the headspace concentrations of three volatiles (isoamyl acetate +, ethyl hexanoate ●, eugenol □) with increasing sucrose concentration in an aqueous matrix.

Table 1
Volatile compounds used and their observed effect values (ratio of headspace concentrations in sugar solutions relative to water) and their predicted values for the original data set (O), the test set (T) and the Volley data set (V)

Data set	Volatile compound	Actual effect	Predicted effect	Data set	Volatile compound	Actual effect	Predicted effect
O	Ethyl decanoate	0.54	0.13	O	Cyclohexanone	1.84	1.90
O	Menthofuran	0.66	0.53	O	Isoamyl acetate	1.89	2.11
O	Ethyl methyl furan	0.71	0.99	O	Diethyl succinate	1.92	2.47
O	Dimethyl sulfide	0.72	0.57	O	Valeronitrile	1.93	1.50
O	2-Isopropyl phenol	0.77	0.92	O	Ethyl acetate	1.98	1.83
O	Benzaldehyde	0.83	1.01	O	Ethyl butyrate	1.99	2.00
O	(E)-2-hexenal	0.88	1.02	O	Hexanol	2.05	2.66
O	Methyl salicylate	0.89	0.91	O	Hexyl acetate	2.07	1.65
O	Anethole	0.96	0.74	O	Butanone	2.14	1.76
O	Acetaldehyde	1.05	0.96	O	1,4-Cineole	2.18	2.33
O	Furan	1.11	1.17	O	Furfuryl acetate	2.21	2.19
O	2,5-Dimethylpyr.[a]	1.14	1.53	O	Terpinolene	2.22	1.64
O	Eugenol	1.16	1.42	O	Linalool	2.46	2.72
O	Octan-2-one	1.23	1.34	O	Caryophyllene	2.65	0.08
O	Hexan-2-one	1.24	1.47	T	α-Damascenone	0.67	0.91
O	Isobutyl thiazole	1.31	0.88	T	2, 3-Diethyl pyr.[a]	0.91	1.24
O	Acetylthiophene	1.32	1.40	T	2, 6-Dimethyl cych.[a]	0.98	1.16
O	Menthone	1.33	1.05	T	Heptyl acetate	1.13	1.48
O	Guaiacol	1.34	1.51	T	Pentan-3-one	1.25	1.60
O	Pyrazine	1.37	0.78	T	Isoamylbutyrate	1.28	1.69
O	2-Ibutyl 3-meo pyr.[a]	1.45	1.35	1	Methyl acetate	1.29	1.66
O	Ethyl hexanoate	1.50	1.82	T	3-Ethyl, 2-methyl pyr.*	1.34	1.32
O	Diacetyl	1.64	1.85	1	Ethyl pentanoate	1.42	1.82
O	Acetone	1.72	1.83	1	Pyrrole	1.54	1.79
O	Ethanol	1.80	2.28	V	Acetone	1.50	1.83
O	Methylfuran	1.81	1.30	V	Octanol	1.71	2.53

[a] Abbreviations: pyr- pyrazine, cych- cylohexanone.

and mobility of each volatile compound. It was anticipated that some of these would be related to the partitioning behaviour of the aroma compounds in the sucrose/water solutions. Some of the descriptors used and their values for six of the compounds are shown in Table 2.

Principal component analysis (PCA) was used to identify variables or combinations of variables that explained the relationship between compounds and their effect values. In particular, it was used to show any outliers or samples with undue influence or leverage. Partial least squares regression was used to carry out a multivariate regression analysis of the effect values and the physicochemical descriptors. Descriptors with the largest regression coefficients (highest correlation) were selected from the optimum number of principal components as potential descriptors for further modelling. Eight descriptors were modelled in Design Expert; descriptors were either retained or rejected from the model on the basis of their statistical significance. Additionally, descriptors were tested for co-correlation and were found to have low correlation with other descriptors. This resulted in a quadratic model containing seven linear descriptors plus a quadratic term, which accounted for the observed differences in the effect values.

Table 2
An example of the descriptors used for each volatile compound, where log *P* is the octanol:water partition coefficient, GC hydroxyl is the count of –OH groups in a molecule and SASA is the solvent accessible surface area

Volatile compound	Molecular weight (g/mol)	Log *P*	Electron affinity (eV)	GC hydroxyl	SASA (cm^3/mol)	Molar refractivity (cm^3/mol)	Ring count
Anethole	148.20	2.79	0.07	0.00	90.21	47.88	1.00
Dimethylpyrazine	108.14	0.72	0.37	0.00	70.25	31.54	1.00
Ethanol	46.07	0.08	−3.33	1.00	42.98	13.01	0.00
Menthone	154.25	3.15	−0.89	0.00	85.20	46.52	1.00
Methyl salicylate	152.15	1.49	0.51	1.00	82.27	39.28	1.00

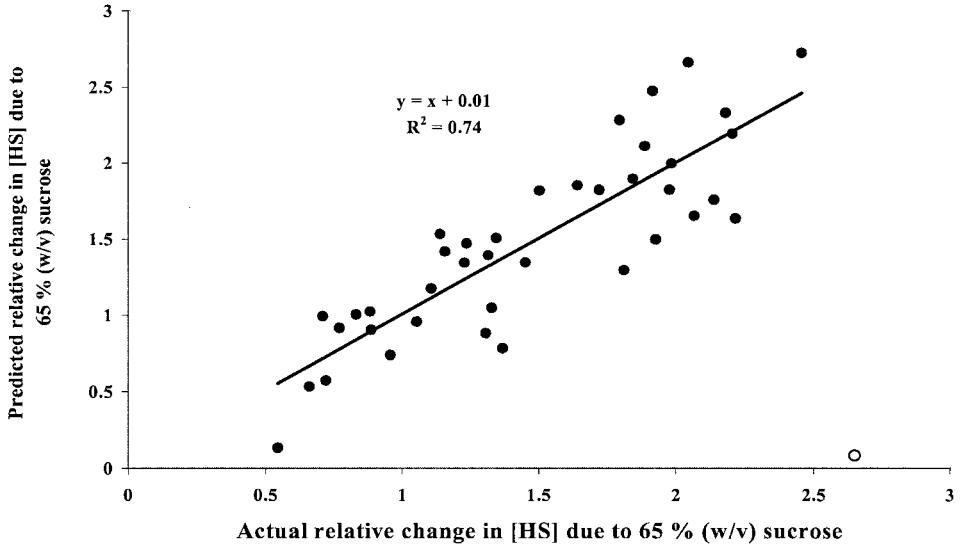

Fig. 2. The actual vs. predicted effect of sucrose on relative headspace concentration for 40 volatiles.

	Effect value =				Prob. > |t|
−	0.350				
−	0.186	*	(log *P* squared)		< 0.0001
+	0.390	*	Carbonyl groupcount		0.0139
+	1.109	*	Connectivity index		0.0030
−	0.102	*	(Connectivity index)^2		0.0319
−	0.110	*	Dipole vector *X*	(Å^3)	0.0237
+	0.604	*	LUMO energy	(eV)	< 0.0001
−	0.562	*	Ring count		0.0029
+	0.116	*	Electrostatic energy	(kcal mol^{-1})	0.0068

(2)

It is important to note that the term $(\log P)^2$ in this equation is one of the mathematical relations to log *P* (the 1-octanol:water partition coefficient), hence it is a linear term and is not making a quadratic contribution to the model.

The *P*-values listed above show the significance of each descriptor in the model. In this case, the significance level, α was 0.05, so descriptors with *P*-values less than 0.05 are significant in the model. All the descriptors in Eq. (2) are, therefore, significant to the model. The values for the Pearson correlation coefficient, R^2, and the cross-validated correlation coefficient, R^2_{cv} for this model were 0.74 and 0.68 (*n* observations = 40) respectively. The cross-validated correlation coefficient is a measure of the predictive capability of the model. The model showed a reasonable linear relationship between the actual relative effect and the predicted effect, (Fig. 2). This model evidently has potential to predict the effect of changing the sucrose concentration on the relative headspace changes, particularly for volatiles that are similar to those used to build the model. The open circle in Fig. 2 shows an outlier from the original data set. This compound was *trans*-caryophyllene, the structure of which is shown in Fig. 3. Caryophyllene was included in the data set in order to extend the range of physicochemical properties, however, in this instance, caryophyllene proved to be a difficult compound to model. It is a particularly water-insoluble compound and more importantly *trans*-caryophyllene is also conformationally unstable. It was not possible to optimise the geometry for this compound prior to generation of the physicochemical descriptors in the CAChe software, thus it is possible that some of the descriptors were incorrectly calculated. These reasons justify the exclusion of this compound from the data set and also provide an indication of the limitations of the QSPR approach.

The size of the coefficients in Eq. (2) depend upon the unit of measure, therefore, it is not possible to assign 'importance' to the descriptors directly. Instead it is necessary to use the 'coded' model produced by the Design Expert software. The coded model has coefficients that are effectively on the same scale, so that coefficients with the highest value are the most important. Lowest unoccupied molecular orbital (LUMO)

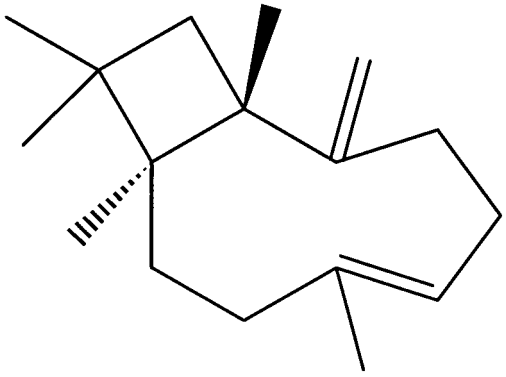

Fig. 3. The structure of caryophyllene, an outlier in the original data set.

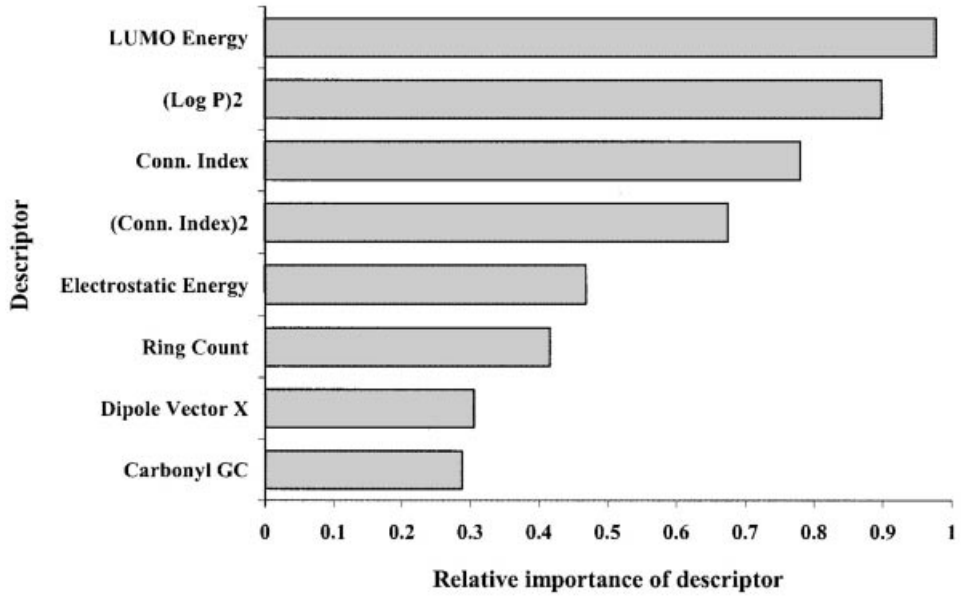

Fig. 4. Relative importance of physicochemical descriptors from the coded model of relative headspace concentration.

energy, log P and a connectivity index term [first order connectivity index (Kier & Hall, 1986)] were the most important descriptors (Fig. 4). It is important to remember that the coded model can not be used with actual values of the physicochemical descriptors to predict the relative headspace concentration, instead Eq. (2) must be used.

Once the most influential descriptors were known, their effects on the relative headspace concentration were visualised by plotting connectivity index against $(\log P)^2$. A contour plot was obtained (Fig. 5) where each contour represents a designated effect value. When predicting the behaviour of compounds from Fig. 5, it is important to remember that the y-axis is $(\log P)^2$. Volatile compounds with low to medium log P values (in the range -1 to 1) are represented in the lower half of the contour plot and compounds with extreme values of log P (greater than 3) are represented in the upper half of the plot. The plot suggests that compounds which are most likely to show a large relative increase in headspace concentration (i.e. high effect values) are those with low values of $(\log P)^2$. This is shown by compounds such as furfuryl acetate [$(\log P)^2 = 0.2$, effect value = 2.2] and butanone ($(\log P)^2 = 1.0$, effect value = 2.1). These ''rules'' for classifying compound behaviour may be related to the observations by Nahon et al. (1998) that the headspace behaviour of volatile compounds in sucrose solutions could be related to their gas chromatography retention time. The x-axis covers a range of values of connectivity indices and as connectivity index is present in the model as a quadratic term as well as a linear term the contours are curved rather than straight lines. Connectivity indices are topological indices, which describe the way in which the atoms of a molecule are bonded together. Topological indices are numeric values associated with chemical constitution for correlation of chemical structure with various physical properties, chemical reactivity or biological activity (van de Waterbeemd et al., 1997). Connectivity indices are, however, very difficult to translate into molecular features (Dearden & James, 1998).

In order to make this model as widely applicable as possible, a diverse set of compounds were used that covered a broad range of physicochemical properties. The model can only be used to predict for compounds in these ranges, i.e. those with connectivity indices greater than 0.71 but less than 6.68. A simultaneous

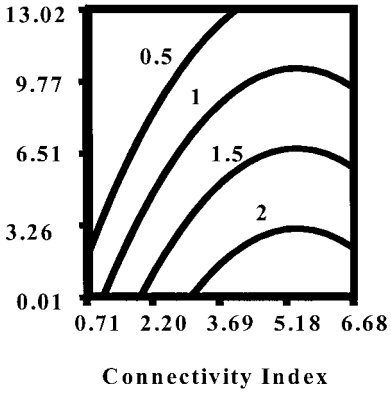

Fig. 5. A contour plot of the two descriptors with greatest importance in the model predicting relative headspace concentration. Each contour line represents an effect value (headspace concentration relative to water; <1 decrease I no change >1 increase in effect value).

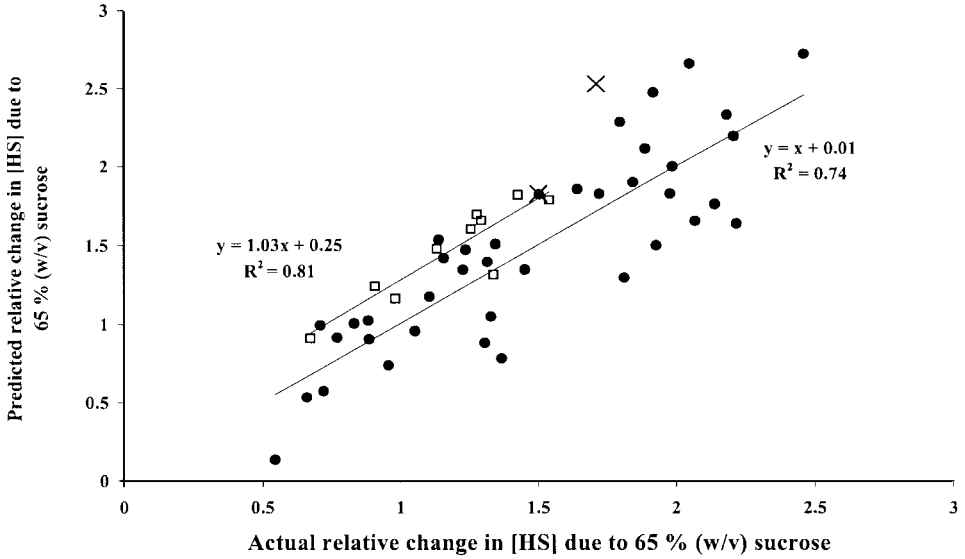

Fig. 6. Predicted versus actual relative changes in headspace concentration (effect value) for the initial data (●), a validation test set (□) and data from the literature (Voilley et al., 1977), (×).

increase in connectivity index and a decrease in $(\log P)^2$ produces an increase in headspace concentration at high sucrose concentrations. In Fig. 5, the contours represent areas of equal relative effect. This indicates that compounds with widely different connectivity indices and log P values can still have the same effect value for 65% (w/v) sucrose.

As well as topological descriptors, the model also contains constitutional descriptors, i.e. those which depend fundamentally on the composition of the molecule rather than on the topology, geometry or electronic structure (Katritzky, Lobanov & Karelson, 1995). Ring count and carbonyl group count are descriptors that reflect the size, and to some extent, the shape of the molecules; these types of descriptors are amongst the easiest to interpret. LUMO energies are related to dispersion energies of polar solutes in solution (Katritzky, Mu & Karelson, 1996), which generally dominate all the interactions between molecules other than hydrogen bonding. Dispersion interactions are directly related to partitioning. However, LUMO energies are quantum chemical descriptors, thus they are more difficult to assign to specific structures or mechanisms, in contrast to hydrophilicity/hydrophobicity descriptors such as log P. The electrostatic energy term reflects the electrostatic structure of the molecules, in particular, the interactions among solutes and the second and third layers of water dipoles arranged around them (Bodor & Huang, 1992; Parke & Birch, 1999). Dipole vector is also a term that describes the interactions of the volatile molecules with solvent molecules. A number of publications provide further definition of descriptors (Dearden, 1990; Dearden & James, 1998; van de Waterbeemd et al., 1997).

5. Model validation

The model was then tested for predictive capability and stability. An external validation set was prepared to test the predictive power of the model for compounds that had not been previously used for the regression. Ten compounds, which were similar to some of the original compounds, were selected and their corresponding structures were drawn and geometrically optimised, prior to calculation of their physicochemical descriptors in CAChe. The predicted and actual effect values were plotted (Fig. 6) and are shown in Table 1 for the test set compounds. In addition, results from the literature (Voilley et al., 1977) were also used as validation data to plot against predictions by the model. The model successfully predicted the relative effect of a 65% (w/v) sucrose solution on the headspace concentration of a test set of 10 volatiles as well as the literature data. The R^2 value for the test set was 0.81.

From the data presented above, it is clear that the model describes the overall partition behaviour of volatile compounds in the presence of 65% sucrose. In terms of QSPR models the fit is adequate (>0.7) but there is obviously some error in the prediction of the effect values. Potential sources of error are the experimental headspace measurements and/or the accuracy of the descriptor values calculated by the software package. Equilibrium headspace measurements varied by 12% but determining the error in the calculated descriptor values is not an easy task. One point to bear in mind is that, ultimately, the reason for measuring these headspace concentration changes is to determine whether they affect the sensory perception of the product. In the literature, various values have been published showing

that it is necessary to change the concentration of a volatile by between 10 and 50% for a sensory change to be noted in a trained panel (Coren et al., 1999). Thus the error in the QSPR model should be judged against the sensory values.

The model conflnns that QSPR can be used to model the interactions of flavour chemicals with their environment, despite the diverse nature of the chemicals themselves; indeed many QSPR models are constructed from data sets of similar compounds. The model also shows the limitations of QSPR in terms of accuracy and the fact that some compounds like *trans*-caryophyllene are not amenable to QSPR modelling. The main advantages of this empirical approach are that it is not necessary to know or even investigate the mechanisms that control the change in headspace concentration with different sucrose concentrations to obtain a model. However, from inspection of the key descriptors in the model, some notion of potential mechanisms can be gleaned. Also, the amount of experimental work required is minimal with all descriptor values generated through software.

Acknowledgements

This research was funded through a Biotechnology and Biological Sciences Research Council CASE studentship with Nestec York Ltd., U.K.

References

Argese, E., Bettiol, C., Giurin, G., & Miana, P. (1999). Quantitative structure–activity relationships for the toxicity of chlorophenols to mammalian submitochondrial particles. *Chemosphere, 38*, 2281–2292.

Bodor, N., & Huang, M. J. (1992). A new method for the estimation of the aqueous solubility of organic compounds. *Journal of Pharmaceutical Sciences, 81*, 954–960.

Coren, S., Ward, L. M., & Enns, J. T. (1999). *Sensation and perception.* Fort Worth: Harcourt Brace.

Dearden, J. C. (1990). Physico-chemical descriptors. In W. Karcher, & J. Devillers, *Practical applications of quantitative structure–activity relationships (QSAR) in environmental chemistry and toxicology* (pp. 25–59). Brussels: ECSC.

Dearden, J. C. (1996). QSAR prediction of Henry's law constant. *Abstracts of Papers of theAmerican Chemical Society, 211*, 53.

Dearden, J. C., Cronin, M. T. D., Ahmed, S. A., & Sharra, J. A. (2000). QSPR prediction of Henry's law constant: Improved correlation with new parameters. In K. Gundertofte, & F. S. Jørgensen, *Molecular modelling and prediction of bioactivity* (pp. 273–274). New York: Plenum Press.

Dearden, J. C., Cronin, M. T. D., Sharra, J. A., Higgins, C., Boxall, A. B. A., & Watts, C. D. (1997). The prediction of Henry's law constant: A QSPR from fundamental considerations. In F. Chen, & G. Schuurmann, *Quantitative structure–activity relationships in environmental sciences* (pp. 135–142). Florida, USA: Society of Environmental Toxicology and Chemistry.

Dearden, J. C., & James, K. C. (1998). Quantitative structure–activity relationships and drug design. In H. J. Smith, *Introduction to the principles of drug design and action* (pp. 167–207). Australia: Harwood Academic Publishers.

De Roos, K. B., & Wolswinkel, K. (1994). Non-equilibrium partition model for predicting flavour release in the mouth. In H. Maarse, & D. G. Van der Heij, *Trends in flavour research* (pp. 15–32). Amsterdam: Elsevier Science.

Ghose, A. K., Pritchett, A., & Crippen, G. M. (1988). Atomic physicochemical parameters for three dimensional structure directed quantitative structure–activity relationships III: modelling hydrophobic interactions. *Journal of Computational Chemistry, 9*, 80–90.

Hills, B. P., & Harrison, M. (1995). Two-film theory of flavour release from solids. *International Journal of Food Science and Technology, 30*, 425–436.

Katritzky, A. R., Lobanov, V. S., & Karelson, M. (1995). QSPR: The correlation and quantitative prediction of chemical and physical properties from structure. *Chemical Society Reviews, 24*, 279–287.

Katritzky, A. R., Mu, L., & Karelson, M. (1996). A QSPR study of the solubility of gases and vapors in water. *Journal of Chemical Information and Computer Sciences, 36*, 1162–1168.

Katritzky, A. R., Wang, Y., Sild, S., & Tamm, T. (1998). QSPR studies on vapour pressure, aqueous solubility and prediction of water-air partition coefficients. *Journal of Chemical Information and Computer Sciences, 38*, 720–725.

Kieckbusch, T. G., & King, C. J. (1979). Partition coefficients for acetates in food systems. *Journal of Agriculture and Food Chemistry, 27*, 504–507.

Kier, L. B., & Hall, L. H. (1986). *Molecular connectivity in structure–activity analysis.* New York: John Wiley and Sons.

Land, D. G., & Reynolds, J. (1981). The influence of food components on the volatility of diacetyl. In P. Schreier, *Flavour '81* (pp. 701–705). Berlin: Walter de Gruyter.

Lien, E. J., & Gao, H. (1995). QSAR analysis of skin permeability of various drugs in man as compared to in-vivo and in-vitro studies in rodents. *Pharmaceutical Research, 12*, 583–587.

Linforth, R. S. T., Friel, E. N. & Taylor, A. J. (in press). Modeling flavor release from foods using physicochemical parameters. In D. D. Roberts, & A. J. Taylor, *Flavor release: Linking experiments, theory and reality*. Washington, DC: American Chemical Society.

Marin, M., Baek, I. & Taylor, A. J. (in press). Flavor release as a unit operation: a mass transfer approach. In D. D. Roberts, & A. J. Taylor, *Flavor release: Linking experiments, theory and reality*. Washington, DC: American Chemical Society.

Mihara, S., & Masuda, H. (1988). Structure–odor relationships for disubstituted pyrazines. *Journal ofAgricultural and Food Chemistry, 36*, 1242–1247.

Nahon, D. F., Koren, P., Roozen, J. P., & Posthumus, M. A. (1998). Flavor release from mixtures of sodium cyclamate, sucrose and an orange aroma. *Journal of Agricultural and Food Chemistry, 46*, 4963–4968.

Overbosch, P., Afterof, W. G. M., & Haning, P. G. M. (1991). Flavour release in the mouth. *Food Reviews International, 7*, 137–184.

Parke, S. A., & Birch, G. G. (1999). Solution properties and sweetness response of selected bulk and intense sweeteners. *Journal of Agricultural and Food Chemistry, 47*, 1378–1384.

Plug, H., & Haring, P. (1994). The influence of food-ingredient interactions on flavor perception. *Food Quality Preference, 5*, 95–102.

Reid, R. C., Prausnitz, J. M., & Poling, B. E. (1987). *Properties of gases and liquids.* New York: McGraw Hill.

Sixt, S., Altschuh, J., & Bruggemann, R. (1995). Quantitative structure toxicity relationships for 80 chlorinated compounds using quantum chemical descriptors. *Chemosphere, 30*, 2397–2414.

Stewart, J. J. P. (1990). MOPAC 6.0.

Taylor, A. J. (1998). Physical chemistry of flavour. *International Journal of Food Science and Technology, 33*, 53–62.

Taylor, A. J. (1999). Flavour matrix interactions. In K. A. D. Swift,

Current topics in flavours and fragrances: Towards a new millenium of discovery (pp. 123–138). The Netherlands: Kluwer Academic.

Taylor, A. J., Linforth, R. S. T., Harvey, B. A. & Blake, A. (2000). Atmospheric pressure chemical ionisation for monitoring of volatile flavour release in vivo. Manuscripts submitted for publication.

van de Waterbeemd, H., Carter, R. E., Grassy, G., Kubinyi, H., Martin, Y. C., Tute, M. S., & Willett, P. (1997). Glossary of terms used in computational drug design. *Pure and Applied Chemistry, 69*, 1137–1152.

Voilley, A., Simatos, D., & Loncin, M. (1977). Gas phase concentration of volatiles in equilibrium with a liquid aqueous phase. *Lebensmittel Wissenschaft Technologie, 10*, 45–49.