Determination of Hansen Solubility Parameters of Solid Materials by Inverse Gas–Solid Chromatography

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Summary. The concept of the solubility parameter has been used in many industries for explanation of the different properties of the components of a formulation. Knowledge of solubility-parameter data for different species is important for predicting the magnitude of interactions between the components of the formulation and for predicting the stability of the product. Determination of Hansen solubility parameters (HSP) for solid materials is extremely complicated. Inverse gas–solid chromatography has been found useful for determination of the HSP of solid polymers and other materials. Use of this technique for characterization of modified and unmodified nanomaterials is presented and discussed.

Introduction

During examination of the properties of the surface layers of materials one seeks a wide range of information, for example surface energy, roughness, likelihood of different intermolecular interactions, and electronic and atomic structure. It has, however, been found that the applicability of these data to solving technical problems might be described as being reversely ordered [1]. In such a situation one must decide which surface properties will describe the behavior of the examined material in a real system sufficiently accurately.

Inverse gas chromatography (IGC) is one technique proposed for examination of the surface properties of solid materials under different conditions (temperature, humidity). IGC is an extension of conventional gas chromatography [2–5]. The word ‘inverse’ means that the examined material is placed in the chromatographic column and its properties are determined by study of the retention behavior of carefully selected test compounds. IGC has been used, for example, for determination of the acid–base ($K_A$ and $K_D$) and dispersive ($\gamma_D^D$) properties of the surface layers of
materials including polymers, conducting polymers, and glass-ionomer cements [2, 3, 6–11].

\( \gamma_S^D \) can be determined by several methods. One of the most often used is that proposed by Schultz and Lavielle [2, 3]. Retention data for series of test \( n \)-alkanes are used to calculate \( \gamma_S^D \) values by use of the equation:

\[
RT \ln V_N = 2Na \sqrt{\frac{R}{\gamma_S^D}} + C
\]

where \( R \) is the gas constant, 8.314 J mol\(^{-1}\) K\(^{-1}\), \( T \) the measurement temperature (K), \( V_N \) the net retention volume (m\(^3\)), \( N \) is Avogadro’s number, 6.023 \( \times \) 10\(^{23} \) (mol\(^{-1}\)), \( a \) the cross-sectional area of the adsorbate (m\(^2\)); \( \gamma_S^D \) the dispersive component of surface free energy (mJ m\(^{-2}\)), \( \gamma_L^D \) the dispersive component of the surface tension of the probe molecule in the liquid state (mJ m\(^{-2}\)), and \( C \) is a constant.

Solubility parameter data are useful for description and interpretation of different phenomena occurring between materials, for example miscibility, compatibility, or adsorption. The Hildebrand solubility parameter, or Hildebrand parameter [12], which can be applied to regular solutions only, is given by:

\[
\delta = (E_{coh} / V)^{1/2}
\]

where \( E_{coh} \) is the cohesive energy and \( V \) is the molar volume. It describes the magnitude of the forces holding the molecules of a liquid together. The solubility parameter can be expressed in the units (cal cm\(^{-3}\))\(^{1/2}\), (J m\(^3\))\(^{1/2}\), MPa\(^{1/2}\), or atm\(^{1/2}\).

The so-called Hansen solubility parameter (HSP) [13] is an extension of the Hildebrand solubility parameter to polar and hydrogen-bonding systems. Hansen assumed that cohesive energy can be regarded as a sum of contributions from dispersive (\( E_d \)), polar (\( E_p \)), and hydrogen-bonding (\( E_h \)) interactions:

\[
-E_{coh} = -E_d - E_p - E_h
\]

and the total solubility parameter (\( \delta_T \)) is expressed as:

\[
\delta_T^2 = \delta_d^2 + \delta_p^2 + \delta_h^2
\]

where \( \delta_d \), \( \delta_p \), and \( \delta_h \) denote the dispersive, polar, and hydrogen-bonding contributions, respectively. The HSP may be determined by different
methods, including IGC, in which the examined material is liquid at the temperature of the experiment.

For solids, determination of solubility parameters by use of eq. (2) is impossible, so indirect methods must be used to estimate their energy of interaction by use of a series of carefully chosen model compounds. Several methods have been used, including densitometry, measurement of solubility by use of Martin’s solution model, and calculation of the solubility parameter by the group contribution method [14]. Determination of solubility parameters for solid materials by inverse gas chromatography is based on the model of adsorption described by Snyder and Karger and requires knowledge of the adsorption energy of the respective test solutes [15–17].

According to the Snyder–Karger model [16] a molecule of test solute ‘i’ is adsorbed by the surface of solid adsorbent ‘j’. From the energy balance, the expression:

\[-\Delta E_A = V_i \left( E_{ij} \right) = V_i \left( E_{ii} \right)^{1/2} \left( E_{jj} \right)^{1/2} = V_i \left( \delta_i \delta_j \right) \]  

(5)

is derived for the energy of adsorption \( \Delta E_A \), where \( V_i \) is the molar volume of the test solute, \( E_{ii} \) and \( E_{jj} \) are the densities of the energy of cohesion of test solute ‘i’ and adsorbent ‘j’, and \( E_{ij} \) is the density of the energy of interaction.

Introducing the Hansen concept of solubility parameter:

\[-\Delta E_A = V_i \left( E_{ij} \right)_d + \left( E_{ij} \right)_p + \left( E_{ij} \right)_h \]  

(6)

or

\[-\Delta E_A = V_i \left( \delta_i \delta_j \right)_d + \delta_i \delta_j + \delta_i \delta_j \]  

(7)

The energy of adsorption is related to the specific retention volume by the equation:

\[ \ln V_g = -\left( \frac{\Delta E_A}{RT} \right) + \text{const} \]  

(8)

When \( N \) test solutes are used in IGC experiments one obtains a system of \( N \) equations corresponding to eq. (7) shown below as a matrix:
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\[ -\Delta E_i = V_i \delta_{id} + V_i \delta_{ip} + V_i \delta_{ih} + \beta_i + \epsilon_i \]

\[ \ldots \]

\[ -\Delta E_n = V_n \delta_{id} + V_n \delta_{ip} + V_n \delta_{ih} + \beta_n + \epsilon_n \]

\[ \ldots \]

\[ -\Delta E_N = V_N \delta_{id} + V_N \delta_{ip} + V_N \delta_{ih} + \beta_N + \epsilon_N \]

\[ \mathbf{Y} = \mathbf{X\beta} + \mathbf{\epsilon} \]

where \( \mathbf{Y} \) is the column vector containing the \( N \) values of experimental measurements of the energy of adsorption (\( -E_n \)) of the \( N \) solutes, \( \mathbf{X} \) is the experimental matrix, formed of elements \( (X_{nk}) \), where \( X_{nk} = V_n \delta_{nk} \), \( V_n \) is the molar volume of the \( n \)th solute, and \( \delta_{nk} \) is one of the Hansen solubility parameters of type \( k \) (where \( k = d, p, \) or \( h \)) of the respective solute. The \( \beta \) vector contains the real values of HSP of the adsorbent, i.e. \( \delta_{jd}, \delta_{jp}, \) and \( \delta_{jh} \), and \( \epsilon \) is the error vector.

In sedimentation methods different solvents are used and good compatibility is usually observed not by one but many different solvents having different values of the three-dimensional solubility parameters [18–21].

Determination of the strength of the interactions between the solid material and the test solvent is performed by observation of the sedimentation and/or suspension of solid particles and/or observation of the intensity of color of the suspensions. Such characterization is based on relatively stronger adsorption of the solid material by some liquids than by others [22]. Test solvents are then classified depending on the extent of sedimentation:

(i) ‘bad’ solvent – rapid sedimentation, no visible effect; and
(ii) ‘good’ solvent – high stability, visible coloring.

Determination of the magnitude of the interactions between the solid material and the test solvent can be performed visually and/or by measurement of absorption, immediately after preparing the dispersions and then again after 24 h. The compatibility region of the solid material and test solvent can be regarded as a sphere of radius \( R \) with the centre located at the point with the dispersive (\( \delta_d \)), polar (\( \delta_p \)), and hydrogen-bonding (\( \delta_h \)) components as coordinates (Fig. 1). These coordinates are defined as the three-dimensional solubility parameters of the solid material examined.
The objective of the work discussed in this paper was estimation of HSP for different solid materials used in the pharmaceutical and food industries.

**Experimental**

**Materials**

The samples examined were:

(i) Ibuprofen (Bayer, Germany), an ingredient of analgesic drugs such as Ibuprofen, Advil, Motrin, Nuprin, and Medipren;
(ii) the nanomaterial Aerosil 200V (Degussa);
(iii) sediment from an aqueous suspension containing 5% (w/w) Aerosil 200V;
(iv) sediment from an aqueous suspension containing 10% (w/w) Aerosil 200V;
(v) sediment from an aqueous suspension containing 15% (w/w) Aerosil 200V;
(vi) sediment from an aqueous suspension containing 20% (w/w) Aerosil 200V;
(vii) the nanomaterial goethite (α-Fe₂O₃) (BASF);
(viii) samples of goethite modified with of poly(acrylic acid) (PAA); and
(ix) poly(acrylic acid) (Fluka).
IGC was used in examination materials (i)–(vii) whereas the sedimentation method was used for characterization of samples (vii)–(ix).

**IGC Experiments**

The samples were packed into a chromatographic column for the IGC experiments. The inverse gas chromatograph was the iGC-SMS from Surface Measurement Systems (UK), with flame ionization detection (FID). Helium was used as carrier gas at a flow rate of 10 mL min$^{-1}$. The column temperature was 293, 303, 313, or 323 K and the detector and injector temperature was 423 K. The mass of stationary phase varied between 0.13 and 0.17 g for Aerosil 200V and 0.36 and 0.39 g for Ibuprofen; these were packed into 2 mm i.d. glass columns. Goethite samples (0.25–0.31 g) were packed into 3 mm i.d. silanized glass columns.

The test compounds were hexane, heptane, octane, nonane, ethanol, propan-1-ol, butan-2-one, pentane-2-one, 1,4-dioxane, acetonitrile, nitropropane, 1,2-dichloroethane, and chloroform. The amount of test solute injected was calculated to enable work in the region of infinite dilution. The dead time was determined by injection of methane.

Chromat-PUT software (prepared during the FP-6 Proform project) was used for calculation of the dispersive component of the surface free energy. Calculations of HSP from retention data collected in gas–solid IGC experiments were performed, by use of Microsoft Excel, in accordance with the Karger–Snyder procedure described in the Introduction.

**Sedimentation Method**

Suspensions of goethite and modified goethite samples were prepared by vigorous shaking and kept at room temperature for 24 h. Absorption measurements were then performed in the range 380–780 nm.

Solvents forming suspensions with absorption <0.2 were classified as ‘bad’ solvents whereas those with absorption >0.2 were classified as ‘good’ solvents.

A set of points for different, ‘good’ test solvents forms, in three-dimensional space, a compatibility region (sphere) with the centre located at coordinates $\delta_d'$, $\delta_p'$, and $\delta_h'$ (Fig. 1). These coordinates are defined as three-dimensional solubility parameters for the materials examined. Calculations were performed by use of a procedure written in-house using Mathcad 12.
Results and Discussion

The activity of the active material in a pharmaceutical composition is crucial to the stability of the final product, i.e. the drug. Solubility parameters can be related to many different physicochemical characteristics and used, for example, for interpretation of such phenomena as miscibility, solubility, and adsorption [23–25]. Solubility parameters are therefore used in the design of pharmaceutical dosage forms [26]. One such active component is Ibuprofen. Hansen solubility parameters for Ibuprofen determined by IGC are listed in Table I.

Table I. HSP values for Ibuprofen

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (MPa(^{1/2}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\delta_d)</td>
<td>12.9 ± 0.2*</td>
</tr>
<tr>
<td>(\delta_p)</td>
<td>6.3 ± 0.8</td>
</tr>
<tr>
<td>(\delta_h)</td>
<td>12.3 ± 0.9</td>
</tr>
<tr>
<td>(\delta_T)</td>
<td>18.9 ± 0.5</td>
</tr>
</tbody>
</table>

* Standard deviation for a confidence level, \(\alpha\), equal to 0.05

The values indicate that Ibuprofen is a relatively active material with a strong tendency to act in hydrogen-bonding interactions (\(\delta_h = 12.3\)). This is probably because of the presence of the carboxyl group in the molecule.

The polar component of the solubility parameter indicates, however, this material is of medium polarity, despite the phenyl group in the molecule. The low value of \(\delta_d\) (12.9) is probably related to small contribution of the aliphatic parts and the significant effect of carboxyl and phenyl groups in reducing the hydrophobic character of aliphatic chains. The dispersive component of the solubility parameter, \(\delta_d\), was determined with the highest precision (see tables), probably because of the highly symmetrical chromatographic peaks obtained for the alkane test solutes and the lowest dispersion of their retention times (Fig. 2). The polar test solute usually gave symmetrical chromatographic peaks (Fig. 2c) but occasionally slight peak tailing could be observed (Fig. 2d). This led to a greater distribution of retention times and standard deviations in determination of both polar \(\delta_p\) and hydrogen-bonding \(\delta_h\) Hansen solubility parameters.
Fig. 2. IGC SMS chromatograms obtained from selected test solutes with Ibuprofen as stationary phase.
Values of the total solubility parameters are in the same range as those determined by the time-consuming partition coefficient method and/or the additive Hoftyzer–van Krevelen procedure (Table II).

**Table II.** Comparison of solubility parameter values obtained for Ibuprofen by use of different methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Solubility parameter (MPa(^{1/2}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGC</td>
<td>18.9 ± 0.5(^a)</td>
</tr>
<tr>
<td>Partition coefficient(^b)</td>
<td>20.8 ± 1.2</td>
</tr>
<tr>
<td>Hoftyzer/van Krevelen(^c)</td>
<td>19.4(^d)</td>
</tr>
<tr>
<td>Hancock [26]</td>
<td>20.2(^d)</td>
</tr>
</tbody>
</table>

\(^a\) Standard deviation for a confidence level, \(\alpha\), equal to 0.05  
\(^b\) Unpublished data from R. Bellingahusen (BTS)  
\(^c\) Additive method  
\(^d\) No precision data available

Use of inverse gas–solid chromatography enables estimation of the activity of this drug at any temperature, for example that of the human body or ‘room’ temperature, i.e. below and/or at 25°C, which is used during manufacture. These HSP values could be further used to predict the behavior of Ibuprofen in a real system. HSP values calculated by use of additive methods are available for 25°C only. It is also difficult or even impossible to estimate precision in this case. Estimation of HSP by determination of partition coefficients is time-consuming and limited to the temperature of the experiment, e.g. most often 25°C. It cannot, moreover, be used for substances completely insoluble in solvents, e.g. iron oxides.

**Table III.** HSP values (MPa\(^{1/2}\)) obtained by IGC for dry Aerosil 200V and for sediment from a 15% aqueous dispersion of Aerosil 200V

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aerosil 200V dry</th>
<th>Sediment from 15% aqueous dispersion of Aerosil 200V</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\delta_d)</td>
<td>18.0 ± 0.2</td>
<td>16.1 ± 0.2</td>
</tr>
<tr>
<td>(\delta_p)</td>
<td>10.8 ± 0.7</td>
<td>11.2 ± 0.6</td>
</tr>
<tr>
<td>(\delta_h)</td>
<td>9.0 ± 0.8</td>
<td>9.7 ± 0.7</td>
</tr>
<tr>
<td>(\delta_T)</td>
<td>22.8 ± 0.5</td>
<td>21.9 ± 0.4</td>
</tr>
</tbody>
</table>

\(^a\) Standard deviation for a confidence level, \(\alpha\), equal to 0.05

Estimation of HSP for solid materials, for example nanomaterials such as Aerosil 200V and goethite, by determination of partition coefficients is
extremely difficult and leads to significant error because of the very low solubility of both oxides in the solvents commonly used. IGC therefore seems an attractive alternative. The results obtained for both nanomaterials are given in Tables III and IV.

**Table IV.** HSP (MPa$^{1/2}$) values obtained for unmodified goethite from the sedimentation and IGC methods

<table>
<thead>
<tr>
<th>Parameter</th>
<th>IGC</th>
<th>Sedimentation method</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\delta_d$</td>
<td>15.5 ± 0.3</td>
<td>15.3 ± 0.2$^a$</td>
</tr>
<tr>
<td>$\delta_p$</td>
<td>6.2 ± 0.2</td>
<td>8.1 ± 0.5</td>
</tr>
<tr>
<td>$\delta_h$</td>
<td>14.2 ± 0.2</td>
<td>14.8 ± 0.6</td>
</tr>
<tr>
<td>$\delta_T$</td>
<td>22.0 ± 0.2</td>
<td>22.8 ± 0.4</td>
</tr>
</tbody>
</table>

$^a$ Standard deviation for a confidence level, $\alpha$, equal to 0.05

The surface activity of nanomaterials is crucially important during their application in real systems, e.g. pharmaceutical and/or food dispersions. It is well known that nanomaterials placed in any solvent undergo agglomeration with the formation of large agglomerates. This substantially changes the surface activity of the material. Formation of a stable product containing the nanomaterial requires use of an appropriate de-agglomeration procedure. Studies in this field, i.e. selection of the best de-agglomeration conditions, have been conducted by many groups and are supported by, for example, European Frame Programmes. Such work, however, requires knowledge of correct physicochemical data describing the status of the examined material in a real environment. In this work we examined changes of the activity of Aerosil 200V samples. It is evident that the surface properties of Aerosil particles (expressed by the HSP and/or $\gamma_s^D$) are highly dependent on the composition of the suspension (Table III). A lower value of the dispersive component of the HSP was obtained for the sediment from the aqueous Aerosil 200V dispersion containing 15% nanomaterial. Interaction of the solvent molecules, i.e. water, with Aerosil 200V caused a slight increase of $\delta_p$ and $\delta_h$ values. This small increase in the tendency to participate in specific interactions did not, however, compensate for the decrease in total activity leading to a lower value of $\delta_T$. These observations were confirmed by results from determination of the dispersive component of the surface free energy (Fig. 3). Increasing the Aerosil 200V particle content to 15% (w/w) resulted in a decrease of $\gamma_s^D$ values. Further increasing the Aerosil content (i.e. above 15%) did not change the activity of the particles. Such physicochemical data are used in
simulation software which enables prediction of the behavior of the oxide dispersions [27].

One means of promoting de-agglomeration is to use surface-active agents which modify the surface of the particles. The goethite surface was modified by application of a layer of poly(acrylic acid) (PAA) and unmodified and PAA-modified samples of the pigment were examined by both IGC and sedimentation methods. The HSP values obtained by use of these two methods (Table IV) are very similar, and indicative of the relatively high activity of the examined surfaces. One should, however, note the lower value of $\delta_p$ obtained from IGC measurements than from the sedimentation procedure. Modification of goethite with poly(acrylic acid) (PAA) leads to a substantial change of its activity (Fig. 4), which could be monitored by use of HSP from IGC experiments. The presence of poly(acrylic acid) molecules on the goethite surface resulted in an increased tendency to participate in polar and hydrogen-bonding interactions, accompanied by a decrease in the dispersive HSP component. None of these changes alters the total value of the solubility parameter $\delta_T$. By using the chromatographic terms we could say that the polarity of the examined material remains almost unchanged but its selectivity was significantly modified.
Fig. 4. Effect on HSP values of modification of goethite with PAA
Conclusions

Inverse gas chromatography is a useful alternative method for determination of the three-dimensional Hansen solubility parameters of solid materials. The results obtained by this procedure are comparable with those from other methods. The advantages of IGC are:

(i) the possibility of determination of HSP of insoluble materials over a wide range of temperatures;
(ii) materials without defined structure may also be characterized; and
(iii) IGC is much less time-consuming than the sedimentation method, for example.

Acknowledgement

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References

[21] C.M. Hansen, Chemtech, 2, 547 (1972)