ELSEVIER

International Journal of Pharmaceutics 194 (2000) 117–124

international journal of pharmaceutics

www.elsevier.com/locate/ijpharm

The modified extended Hansen method to determine partial solubility parameters of drugs containing a single hydrogen bonding group and their sodium derivatives: benzoic acid/Na and ibuprofen/Na

P. Bustamante [a,*], M.A. Peña [a], J. Barra [b]

[a] *Department of Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Alcalá, Alcalá de Henares, 28871 Madrid, Spain*

[b] *School of Pharmacy, University of Geneva, Quai Ernest-Ansermet 30, 1211 Geneva, Switzerland*

Received 21 June 1999; received in revised form 15 October 1999; accepted 15 October 1999

Abstract

Sodium salts are often used in drug formulation but their partial solubility parameters are not available. Sodium alters the physical properties of the drug and the knowledge of these parameters would help to predict adhesion properties that cannot be estimated using the solubility parameters of the parent acid. This work tests the applicability of the modified extended Hansen method to determine partial solubility parameters of sodium salts of acidic drugs containing a single hydrogen bonding group (ibuprofen, sodium ibuprofen, benzoic acid and sodium benzoate). The method uses a regression analysis of the logarithm of the experimental mole fraction solubility of the drug against the partial solubility parameters of the solvents, using models with three and four parameters. The solubility of the drugs was determined in a set of solvents representative of several chemical classes, ranging from low to high solubility parameter values. The best results were obtained with the four parameter model for the acidic drugs and with the three parameter model for the sodium derivatives. The four parameter model includes both a Lewis-acid and a Lewis-base term. Since the Lewis acid properties of the sodium derivatives are blocked by sodium, the three parameter model is recommended for these kind of compounds. Comparison of the parameters obtained shows that sodium greatly changes the polar parameters whereas the dispersion parameter is not much affected. Consequently the total solubility parameters of the salts are larger than for the parent acids in good agreement with the larger hydrophilicity expected from the introduction of sodium. The results indicate that the modified extended Hansen method can be applied to determine the partial solubility parameters of acidic drugs and their sodium salts.

Keywords: Partial solubility parameters; Benzoic acid; Sodium benzoate; Ibuprofen; Sodium ibuprofen; Extended Hansen method

* Corresponding author. Tel.: +34-91-8854659; fax: +34-91-8854658.
E-mail address: tfpbm@farma.alcala.es (P. Bustamante)

0378-5173/00/$ - see front matter
PII: S0378-5173(99)00374-9

1. Introduction

Sodium salts are often used in drug formulation but their partial solubility parameters are not available. The introduction of sodium greatly changes solubility and other physical properties of the drug and the knowledge of the partial solubility parameters of the sodium salt would help to predict adhesion properties that cannot be estimated using the solubility parameters of the parent acid. Solubility parameters provide a simple method for predicting cohesive and adhesive properties of materials (Barton, 1991). Rowe (1988, 1989) used solubility parameters to predict the adhesion of film coatings to tablets and to obtain interfacial works of adhesion between substrate and binder. The experimental methods to determine partial solubility parameters have not been applied to sodium salts, except for sodium diclofenac (Bustamante et al., 1998b). The extended Hansen method (Martin et al., 1981, 1984; Wu et al., 1982; Beerbower et al., 1984) for determining partial solubility parameters is based upon a regression between $\ln a_2/U$ and the partial solubility parameters of a series of solvents, where a is the activity coefficient of the drug and U is related to the molar volume of the drug and the volume fraction of the solvent. The method uses a model involving the three partial solubility parameters of Hansen, dispersion, dipolar and hydrogen bonding (Hansen, 1967a,b) and a model with four partial parameters (dispersion, dipolar, acidic and basic). The method was used to determine partial solubility parameters of several drugs (Richardson et al., 1992; Subrahmanyam and Suresh 1999). The approach was then modified to directly relate the logarithm of the solubility mole fraction of the drug $\ln X_2$ to the partial solubility parameters of the solvents (Bustamante et al., 1998a,b). The three parameter model is written:

$$\ln X_2 = C_o + C_1\delta_{1d}^2 + C_2\delta_{1d} + C_3\delta_{1p}^2 + C_4\delta_{1p} + C_5\delta_{1h}^2 + C_6\delta_{1h} \quad (1)$$

where δ_d, δ_p and δ_h represent the dispersion, dipolar and hydrogen bonding partial solubility parameters of Hansen (1967a). The four parameter model divides δ_h into the acidic and basic partial solubility parameters of Karger et al. (1976), δ_a and δ_b, representing the proton donor and proton acceptor capability, respectively:

$$\ln X_2 = C_o + C_1\delta_{1d}^2 + C_2\delta_{1d} + C_3\delta_{1p}^2 + C_4\delta_{1p} + C_5\delta_{1a} + C_6\delta_{1b} + C_7\delta_{1a}\delta_{1b} \quad (2)$$

The partial solubility parameters of the drug can be obtained from the regression coefficients of Eq. (1) and Eq. (2):From Eq. (1):

$$\delta_{2d} = -\left(\frac{C_2}{2C_1}\right);$$

$$\delta_{2p} = -\left(\frac{C_4}{2C_3}\right); \text{ and } \delta_{2h} = -\left(\frac{C_6}{2C_5}\right) \quad (3)$$

From Eq. (2):

$$\delta_{2d} = -\left(\frac{C_2}{2C_1}\right); \quad \delta_{2p} = -\left(\frac{C_4}{2C_3}\right);$$

$$\delta_{2a} = -\left(\frac{C_6}{C_7}\right); \text{ and } \delta_{2b} = -\left(\frac{C_5}{C_7}\right) \quad (4)$$

The modified method (Eq. (1) and Eq. (2)) provided more significant parameters than the original extended Hansen method for citric acid (Barra et al., 1997) and weakly acidic drugs, and was also tested with piroxicam, a mainly Lewis-base compound (Bustamante at al., 1998a). The results obtained with sodium diclofenac suggested that the method could also be applied to sodium salts (Bustamante et al., 1998b). To test the suitability of the method for sodium salts, two drugs containing a single hydrogen bonding group, ibuprofen and benzoic acid and their sodium derivatives were chosen.

2. Material and methods

Ibuprofen was kindly supplied by Laboratories UPSA, Agen, France, (batch 49197); sodium ibuprofen, benzoic acid and sodium benzoate were purchased from Sigma Chemical, St Louis, MO, USA. The same solvents (spectrophotometric or analytical grade, Panreac, Monplet, Barcelona, Spain) previously used to determine the partial solubility parameters of anti-inflammatory drugs are employed in this study (Table 1). These solvents represent several chemical classes and cover a wide range of the solubility parameter scale from low (heptane, $\delta_T = 15.33$ MPa$^{1/2}$) to

high (water $\delta_T = 47.86$ MPa$^{1/2}$) solubility parameter values. The water content was determined with the Karl Fisher rapid test, Merck, Germany, (Bustamante et al., 1998b). The solubilities of benzoic acid in the solvents listed in Table 1 were taken from Beerbower et al. (1984) except for 1,2-propanediol, which was determined experimentally to be $X_2 = 0.0872$. The solubility of ibuprofen, sodium ibuprofen and sodium benzoate was measured in the solvents shown in Table 1 as previously reported (Bustamante et al., 1998a). Some of the solvents interferred with the spectrophotometric readings: acetophenone, cyclohexane, *N*,*N*-dimethylformamide, formamide and chlorobenzene for ibuprofen; ethyl acetate, chloroform, benzene, acetophenone, *N*,*N*-dimethylformamide, *N*-methylformamide and chlorobenzene for sodium ibuprofen; and chloroform, ethyl acetate, acetone, cyclohexane, acetophenone, benzene and chlorobenzene for sodium benzoate. These solvents were evaporated before dilution with ethanol 96% for the spectrophotometric assay (Shimadzu UV-2101 PC, Japan). The densities of the solutions were determined at 25 ± 0.1°C in 10 ml pycnometers. The ideal solubility (mole fraction units) was calculated from the heat and temperature of fusion obtained from differential scanning calorimetry (Mettler TA 4000, Switzerland):

$$\ln X_2^i = -\frac{\Delta H_f}{R}\left(\frac{1}{T} - \frac{1}{T_f}\right) \quad (5)$$

The DSC analysis was performed with the original powders and with the solid phase after equili-

Table 1
Experimental solubilities (log mole fraction units) of ibuprofen, sodium ibuprofen and sodium benzoate

Solvents	δ_T[a]	Ibuprofen ln X_2	Sodium ibuprofen ln X_2	Sodium benzoate ln X_2
Ethanol	26.50	−1.9503	−2.5573	−6.5257
Chloroform	18.94	−1.3712	−7.7910	−13.7266
Methanol	29.61	−3.7017	−1.3116	−4.2555
Benzene	18.54	−2.4684	−12.3017	−14.7752
Dioxane	20.47	−3.2918	−8.7174	−14.4960
Acetic acid	21.35	−2.1746	−3.3999	−1.8855
1-Pentanol	21.65	−1.5436	−2.8702	−7.0713
Cyclohexane	16.76	−1.8834	−11.6705	−14.1714
1,2-Propanediol	30.20	−2.4547	−1.4146	−3.9739
Formamide	36.64	−6.5485	−3.8359	−3.1578
Ethylene glycol	32.70	−3.9612	−0.6762	−2.5220
Glycerol	36.07	−5.8932	−1.2651	−2.9214
Ethyl acetate	18.48	−1.0942	−7.3852	−13.0333
Propionic acid	20.67	−1.5611	−3.4886	−1.8922
Ethylene dichloride	20.79	−2.4549	−10.1933	−10.5982
1-Octanol	20.96	−1.5134	−2.7018	−11.8741
Heptane	15.33	−2.8827	−11.2964	−12.3362
Chlorobenzene	19.61	−3.9057	−12.9644	−12.0533
Diethyl ether	15.66	−3.8065	−7.4103	−13.1943
Acetone	19.95	−1.0474	−7.8829	−10.7859
Acetophenone	21.73	−5.7807	−10.0583	−10.3151
N,*N*-Dimethylformamide	24.80	−2.0580	−6.7721	−8.2058
Water	47.86	−13.3980	−3.5326	−2.8553
N-Methylformamide	29.63	–	−6.2656	–
1,4-Butanediol	33.46	–	−1.4053	–
1,3-Propanediol	32.66	–	−2.2121	–

[a] Total solubility parameter (MPa$^{1/2}$). The partial solubility parameters of the solvents are found in Bustamante et al. (1998a). The partial solubility parameters of the new solvents used (MPa1/2) are: 1,3-propanediol $\delta_d = 16.56$, $\delta_p = 10.84$, $\delta_h = 25.97$, $\delta_a = 22.29$, $\delta_b = 15.13$ and $\delta_T = 32.66$; 1,4-butanediol $\delta_d = 16.77$, $\delta_p = 16.56$, $\delta_h = 23.72$, $\delta_a = 37.22$, $\delta_b = 7.56$ and $\delta_T = 33.46$; and N-methylformamide $\delta_d = 17.18$, $\delta_p = 20.65$, $\delta_h = 12.47$, $\delta_a = 9.81$, $\delta_b = 7.97$ and $\delta_T = 29.63$

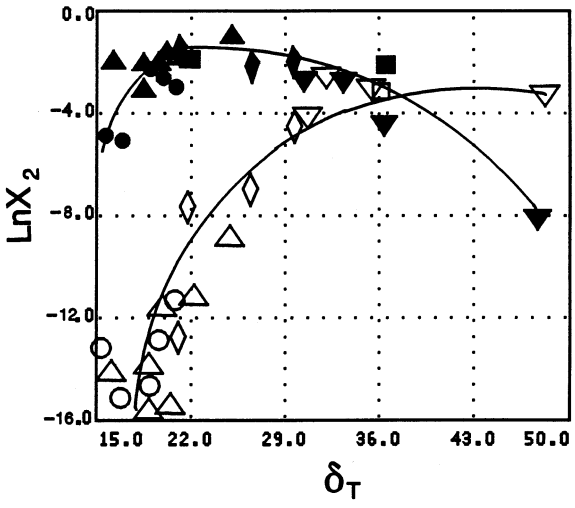

Fig. 1. Experimental log mole fraction solubility of benzoic acid (solid point) and sodium benzoate against the solubility parameter of the solvents: nonpolar (○), bases (△), acids (□), alcohols (◇) and glycols (▽).

bration with the solvents after drying of the samples.

The data were processed with the NCSS 97 statistical package (Hintze, 1997). Residual analysis and the Cook distance was used to detect the solvents that least fitted the models assigning an smaller weight (0.001) to these cases. The weighted regression analysis allows to improve the values of the parameters obtained.

3. Results and discussion

3.1. Solubility behaviour of acidic drugs and sodium derivatives

The water content of the samples was 3.3% for ibuprofen, 13% for sodium ibuprofen, 4.1% for benzoic acid and 4.3% for sodium benzoate. For comparison with sodium benzoate, the solubility profile of benzoic acid (Martin et al., 1984) is also plotted in Fig. 1. The region of maximum solubility is located between 22 and 29 $MPa^{1/2}$. The solubility of benzoic acid in alcohols is larger than in glycols. The carboxylic group may act as a Lewis-base against acidic solvents and as a Lewis-acid against basic solvents. Thus, dioxane as well as acetic and propionic acids are good solvents for benzoic acid. The ideal solubility of sodium benzoate ($X_2^i = 3.8778 \times 10^{-3}$) is lower than for benzoic acid ($X_2 i = 0.1971$) as a result of its larger temperature of fusion and heat of fusion ($T_f =$ 437.4°C, $\Delta H_f = 23.71$ KJ/mol and $T_f = 123.3$°C, $\Delta H_f = 16.23$ KJ/mol, respectively). Owing to strong dipole-dipole interactions, the solubility of the salt increases in water and glycols whereas it decreases in nonpolar solvents and alcohols (Fig. 1). The maximum solubility of the salt is obtained in acidic solvents (acetic and propionic acids). The region of maximum solubility shifts to larger polarity values when compared to the parent acid ($\delta_T = 30–50$ $MPa^{1/2}$).

Ibuprofen is expected to be less polar than benzoic acid because its lipohilic moiety is larger. Accordingly, the highest solubility of ibuprofen is obtained insolvents of lower solubility parameter values such as acetone and ethyl acetate (Lewis bases) and lipophilic alcohols (pentanol and octanol). The carboxylic group of ibuprofen is donor-acceptor and may interact with both the proton-acceptor oxygens of acetone and ethyl acetate and with the acidic proton of alcohols. Solubility decreases in the most polar alcohols

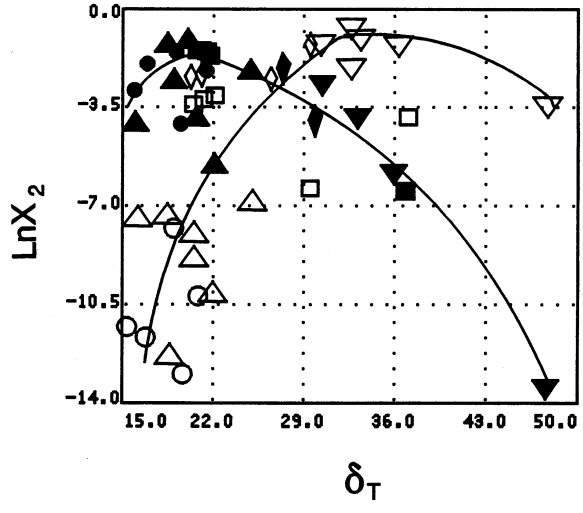

Fig. 2. Experimental log mole fraction solubility of ibuprofen (solid point) and sodium ibuprofen against the solubility parameter of the solvents: nonpolar (○), bases (△), acids (□), alcohols (◇) and glycols (▽).

Table 2
Partial solubility parameters of ibuprofen, sodium ibuprofen, benzoic acid and sodium benzoate (MPa)1/2 from Eqs. Eq. (1) and Eq. (2)[a]

Model	δ_d	δ_p	δ_h	δ_a	δ_b	δ_T	r^2	SD
Ibuprofen								
Three parameters (Eq. (1))	16.44	6.39	8.89	NA	NA	19.75	0.93	0.46
Four parameters (Eq. (2))	16.37	7.67	7.21[b]	5.36	4.85	19.46	0.93	0.45
Sodium ibuprofen								
Three parameters (Eq. (1))	17.50	17.89	29.31	1.43[c]	17.21[d]	38.54	0.98	0.40
Benzoic acid								
Four parameters (Eq. (2))	17.63	10.10	10.74[b]	9.27	8.23	22.98	0.97	0.21
Four parameters[e]	17.26	12.17	11.34	9.83	6.54	22.33	0.83	21.24
Sodium benzoate								
Three parameters (Eq. (1))	16.28	29.19	13.04	1.43[c]	7.71[d]	35.87	0.99	0.23

[a] NA = not applicable
[b] δ_{2h} calculated with Eq. (6), $\delta_h^2 = 2\delta_a\delta_b$.
[c] The value of benzene is assigned _a = 1.43 MPa1/2 (see the text).
[d] Calculated from Eq. (6).
[e] Beerbower et al., 1984, with ln $a2$/U as the dependent variable.

(methanol) and glycols of large δ values (Fig. 2). The replacement of the acidic proton by sodium blocks the Lewis-acid properties, increasing significantly the Lewis-base properties of sodium ibuprofen. The enhancement of basic properties is even more important than in the case of sodium diclofenac which has an additional polar group (Bustamante et al., 1998b). The sodium derivative of ibuprofen is more hydrophilic than the one of diclofenac. The highest solubilities are found in proton-donor solvents such as glycols and water (Fig. 2). As expected, the region of maximum solubility of the sodium derivatives is shifted to larger solubility parameter values compared to the parent acids.

3.2. Partial solubility parameters of ibuprofen and sodium ibuprofen monohydrate

The experimental solubilities of ibuprofen and sodium ibuprofen, expressed as the logarithm of the mole fractions, are listed in Table 1 and were fitted to Eq. (1) and Eq. (2). For comparison, the dependent variables of the original extended Hansen method, (ln α_2/U)cst and (ln α_2/U)var, were also tested with Eq. (1) and Eq. (2). These variables were obtained as previously reported (Bustamante et al., 1998a) and differ in the calculation of the values of α_2, where $\alpha_2 = X_2^i/X_2$. In the case of (ln α_2/U)cst, α is computed from the ideal solubility $X_2 i$ (Eq. (5)) obtained with the heat and temperature of fusion of the original powders (ibuprofen, $X_2^i = 0.2368$ and sodium ibuprofen, $X_2^i = 0.06417$). The heats and temperatures of fusion of the solid phase after equilibration with the solvents listed in Table 1 are used to obtain the values of $\alpha 2$ for (ln $_2/U$)var. The partial solubility parameters of the solvents needed for the regression analysis were previously published (Bustamante et al., 1998a). Some of the regression coefficients were not significant at 95% confidence level with neither (ln $_2/U$)cst nor (ln $_2/U$)var and the values of these variables are not listed in Table 1.

Table 2 shows the partial solubility parameters obtained with the models and dependent variables that gave statistically significant regression coefficients at least at the 95% confidence level. Diethyl ether was the solvent which least fitted the data of ibuprofen although this solvent did not alter the DSC profile. All the other solvents were compatible with the overall regression. The dependent variable ln X_2 provided statistically significant regression coefficients for both the three- and four

parameter models (Eq. (1) and Eq. (2)). The total solubility parameter of ibuprofen ($\delta_T = 19.5$ $MPa^{1/2}$, Table 2) is low, in good agreement with the large lipophilic region compared to the single polar group (-COOH) of the molecule.

The four parameter model did not provide significant regression coefficients for sodium ibuprofen. The reason is that the sodium salt does not contain any proton-donor group whereas the four parameter model includes both proton donor δ_a and proton acceptor δ_b parameters (Eq. (2)). Therefore, the three parameter model (Eq. (1)) was applied. For the drugs previously studied, the region of maximum solubility was located at intermediate solubility parameter values leaving an enough number of solvents at the left and the right part of the plot. However, sodium ibuprofen is much more hydrophilic than these compounds and only three solvents are located at the rigth part of the maximum. As a result, the maximum solubility was not well defined leading to wrong signs on the regression coefficients and negative partial solubility parameters. To solve this problem, the experimental solubilities in three additional solvents of high solubility parameter values, 1,3-propanediol, 1,4-butanediol and *N*-methylformamide were added. With the new polar solvents, all the regression coefficients showed correct signs, according to the three parameter model (Eq. (1)). The solvents which least fitted the model were benzene, dioxane, formamide, ethyl acetate, chlorobenzene, octanol and ethylene glycol. Among these solvents, benzene, chlorobenzene and ethyl acetate interferred with the spectrophotometric readings. Water was fully compatible with the regression model, suggesting that for hydrophilic drugs water can be included in the regression analysis.

The partial solubility parameters of sodium ibuprofen are listed in Table 2. In order to obtain the acidic and basic parameters δ_a and δ_b, the following procedure is suggested. In the solubility parameter scale, the values of δ_a are not zero, even for nonpolar solvents. Since sodium ibuprofen does not contain any Lewis-acid group, the acidic parameter must be very low, much smaller than the basic parameter. Thus the value of δ_a for benzene is assigned to sodium ibuprofen, and δ_b can be estimated from Eq. (6) which relates δ_a and δ_b to δ_h (Karger et al., 1976):

$$\delta_h^2 = 2\delta_a\delta_b \quad (6)$$

The parameters thus obtained are $\delta_a = 1.43$ and $\delta_b = 17.21$ $MPa^{1/2}$.

As observed in Table 2, the total solubility parameter of sodium ibuprofen is larger than that of ibuprofen (38.54 versus 19.46 $MPa^{1/2}$, respectively). The hydrogen bonding parameter is also larger than for the parent acid owing to the increase of the Lewis-base properties ($\delta_{2b} = 17.2$) which is consistent with the much larger solubility of the salt in glycols and water. The total solubility parameter of sodium ibuprofen is also larger than the value obtained for sodium diclofenac (Bustamante et al., 1998b), a less water soluble sodium derivative (29.8 $MPa^{1/2}$).

3.3. Partial solubility parameters of benzoic acid and sodium benzoate

The partial solubility parameters of benzoic acid were determined by Beerbower et al. (1984) in a large set of solvents ($n = 59$), using ($\ln \alpha_2/U$)cst as the dependent variable. These parameters were recalculated with the smaller set of solvents shown in Table 1. With the variable ($\ln \alpha_2/U$)cst the regression coefficient of δ_{1p} was not significant statistically whereas the fit was excellent with $\ln X_2$ (Eq. (2)). Methanol, benzene, ethylene dichloride and formamide were the solvents that least fitted the model although these solvents did not change the DSC profile of benzoic acid. The partial solubility parameters of benzoic acid (Table 2) are very similar to those obtained by Beerbower et al. (1984). This suggests that the modified model (Eq. (2)) allows to reduce the number of experimental solubilities increasing the significance of the parameters obtained. Benzoic acid is more polar than ibuprofen, and its δ_T value is about three units higher owing to the increase of δ_p and δ_h (Table 2). The acidic and basic parameters δ_a and δ_b of benzoic acid are larger than for ibuprofen. The larger values of the polar parameters are consistent with the smaller size of the lipophylic moiety of benzoic acid compared to that of ibuprofen. The acidic parameter

of benzoic acid is larger than the basic parameter ($\delta_a = 9.27$ and $\delta_b = 6.23$ $MPa^{1/2}$) suggesting that this compound is a better Lewis-acid against basic solvents than Lewis-base toward acidic solvents.

Table 1 displays the experimental $\ln X_2$ for sodium benzoate. As for sodium ibuprofen, the sodium ion blocks the Lewis-acid characteristics of benzoic acid, and the four parameter model cannot be applied to sodium benzoate. Acetic acid and propionic acid were totally incompatible with the model, even giving a 0.001 weight and were removed from the regression analysis. These solvents modified the DCS profile of the original powder. The three parameter model associated with $\ln X_2$ provided significant partial solubility parameters. The solvents that least fitted the model were cyclohexane, dioxane, pentanol, glycerol, ethyl acetate, heptane and acetophenone. These solvents did not change the DSC profile of sodium benzoate but cyclohexane, ethyl acetate and acetophenone interferred with the spectrophotometric readings. As expected, the total solubility parameter of sodium benzoate was much larger than the value of the parent acid (35.87 and 22.98 MPa1/2, respectively, Table 2). Sodium significantly enhances the polarity of the molecule. Thus the dipolar parameter δ_p increases from 10.10 to 29.19 $MPa^{1/2}$. The hydrogen bonding parameter does not show a large change (13.04 versus 10.74 $MPa^{1/2}$). Eq. (6) is used to estimate the δ_a and δ_b parameters of sodium benzoate. With $\delta_a = 1.43$ $MPa^{1/2}$ (the value of benzene) and the δ_h obtained from the regression analisis, the calculated value ($\delta_b = 7.71$ $MPa^{1/2}$, Table 2) is quite reasonable as it is larger than of the parent acid.

The results obtained (Table 2) show the large influence of sodium in changing the solubility parameters of the drugs, especially the values of the polar and hydrogen bonding parameters. The values of δ_d are not subtantially affected, whereas δ_p δ_h, and consequently δ_T, are much larger. For sodium drugs that do not contain proton-donor groups such as sodium ibuprofen and sodium benzoate, the three parameter model (Eq. (1)) is preferred and the value of the basic partial solubility parameter can be estimated from the equation of Karger which relates δ_a and δ_b to the Hansen hydrogen bonding parameter δ_h (Eq. (6)). For these kinds of drugs, sodium annihilates the Lewis-acid characteristics of the molecule. For drugs having both proton-donor and proton acceptor groups the four parameter equation (Eq. (2)) is the best model. The results suggests that the modified extended Hansen model is applicable to both acidic drugs and sodium derivatives.

Acknowledgements

This research was supported by the University of Alcala (project no. E007/99)

References

Barra, J., Lescure, F., Doelker, E., Bustamante, P., 1997. The expanded Hansen approach to solubility parameters. Paracetamol and citric acid in individual solvents. J. Pharm. Pharmacol. 49, 644–651.

Barton, A.F.M., 1991. Handbook of solubility parameters and other cohesion parameters. CRC Press, Boca Raton, FL.

Beerbower, A., Wu, P.L., Martin, A., 1984. Expanded solubility parameter approach. I. Naphthalene and benzoic acid in individual solvents. J. Pharm. Sci. 73, 179–188.

Bustamante, P., Peña, M.A., Barra, J., 1998a. Partial solubility parameters of piroxicam and niflumic acid. Int. J. Pharm. 174, 141–150.

Bustamante, P., Peña, M.A., Barra, J., 1998b. Partial solubility parameters of naproxen and sodium diclofenac. J. Pharm. Pharmacol. 50, 975–982.

Hansen, C.M., 1967a. The three dimensional solubility parameter-key to paint components affinities. I. Solvents, plasticizers, polymers and resins. J. Paint. Tech. 39, 104–117.

Hansen, C.M., 1967b. The three dimensional solubility parameter-key to paint components affinities. II and III. Dyes, emulsifiers, mutual solubility and compatibility, and pigments. J. Paint. Tech. 39, 511–514.

Hintze, J.L., Number cruncher statistical system, 1997. Kaysville, Utah.

Karger, B.L., Snyder, L.R., Eon, C., 1976. An expanded solubility parameter treatment for classification and use of chromatographic solvents and adsorbents: parameters for dispersion, dipole and hydrogen bonding interactions. J. Chromatogr. 125, 71–88.

Martin, A., Wu, P.L., Adjei, A., Beerbower, A., Prausnitz, J.M., 1981. Extended Hansen solubility approach: naphtalene in individual solvents. J. Pharm. Sci. 70, 1260–1264.

Martin, A., Wu, P.L., Beerbower, A., 1984. Expanded solubility parameter approach. II. *p*-Hydroxybenzoic acid and methyl *p*-hydroxybenzoate in individual solvents. J. Pharm. Sci. 73, 188–194.

Richardson, P.J., McCafferty, D.F., Woolfson, A.D., 1992. Determination of the three-component partial solubility parameters for temazepam and the effects of change in partial molal volume on the thermodynamics of drug solubility. Int. J. Pharm. 78, 189–198.

Rowe, R.C., 1988. Adhesion of film coatings to tablet surfaces a theoretical approach based on solubility parameters. Int. J. Pharm. 41, 219–222.

Rowe, R.C., 1989. Binder-substrate interactions in granulation: a theoretical approach based on surface free anergy and polarity. Int. J. Pharm. 52, 149–154.

Subrahmanyam, C.V.S., Suresh, S., 1999. Solubility behavour of haloperidol in individual solvents. Determination of partial solubility parameters. Eur. J. Pharm. Sci. 47, 289–294.

Wu, P.L., Beerbower, A., Martin, A., 1982. Extended Hansen approach: calculating partial solubility parameters. J. Pharm. Sci. 71, 1285–1287.