

## Research Article

# Surface Characterization of Phenylpropanolamine Drug by Inverse Gas Chromatography

**B. Praveen Kumar, P. Reddi Rani, T. Madhusudana Reddy, and K. S. Reddy**

*Department of Chemistry, Sri Venkateswara University, Tirupati, Andhra Pradesh 5/7 502, India*

Correspondence should be addressed to K. S. Reddy; [ksreddy01@rediffmail.com](mailto:ksreddy01@rediffmail.com)

Received 10 June 2013; Accepted 15 July 2013

Academic Editors: D. Knopf, E. B. Starikov, and E. Yeow

Copyright © 2013 B. Praveen Kumar et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The surface thermodynamic properties can be used to understand the interactive potential of a drug surface with a solid or liquid excipient during its formulation and drug release process. The retention data were measured for n-alkanes and polar solutes at intervals of 5 K in the temperature range 318.15–333.15 K by Inverse Gas Chromatography (IGC) on the solid surface of phenylpropanolamine (PPA) drug. The retention data were used to evaluate the dispersive surface free energy,  $\gamma_s^d$ , and Lewis acid-base parameters,  $K_a$  and  $K_b$ , for the PPA drug. The values,  $\gamma_s^d$ , were decreasing linearly with increase of temperature and at 323.15 K the value was found to be  $26.01 \pm 0.40$  mJ/m<sup>2</sup>. The specific components of enthalpy of adsorption of polar solutes have been applied to evaluate Lewis acid-base parameters. The  $K_a$  and  $K_b$  values were found to be  $0.451 \pm 0.033$  and  $0.824 \pm 0.622$ , respectively, which suggests that the PPA surface contains more basic sites and interact strongly in the acidic environment.

## 1. Introduction

The surface energetics of a pharmaceutical solid will influence its interaction with another solid or liquid when it is in close contact. An interfacial energy will be developed at the interface when two such condensed systems interact. The magnitude of this interfacial energy depends on the individual surface energies of the two systems. The interfacial energy will influence several factors such as wetting and spreading of a liquid over a solid surface, binding of a film to a tablet, wet granulation, and dissolution and suspension formulation of a drug during processing [1–9]. Several techniques are available to measure surface energetics of a solid; however, the IGC method has been proved to be more effective and simple technique [10–15].

In the IGC method n-alkanes and polar probes are injected at infinite dilution on a column packed with pharmaceutical material. The surface free energy of a pharmaceutical solid is often divided into two components dispersive and specific. The dispersive surface energy is usually investigated by using the retention data of n-alkane solutes and the specific interaction ability of the surface has been studied using the data of polar solutes. The comparison of the retention

property of the polar solutes with the n-alkanes will result in the evaluation of Lewis acidity,  $K_a$ , and Lewis basicity,  $K_b$ , parameters.

The purpose of this paper is to determine the surface thermodynamic properties of PPA drug by IGC method. The dispersive surface free energy at four temperatures and Lewis acid-base parameters for the solid PPA surface has been reported. PPA is an important drug which can be used to cure respiratory illness and the properties reported here may be utilized during its formulation. A literature survey revealed that the surface properties of PPA have not been studied earlier.

## 2. IGC Theory

The net retention volumes,  $V_N$ , can be calculated according to the following equation:

$$V_N = (t_R - t_0) FJ \left( \frac{P_o - P_W}{P_o} \right), \quad (1)$$

where  $t_R$  is the retention time of the probe solute,  $t_0$  is the retention time of methane,  $F$  is the flow rate of the carrier

gas,  $P_W$  is the saturate vapour pressure of water at ambient temperature,  $P_o$  is the atmospheric pressure, and  $J$  is the James and Martin pressure correction factor.

According to Schultz et al. [15] the dispersive surface free energy,  $\gamma_s^d$ , is related to the net retention volume as follows:

$$RT \ln V_N = 2 Na (\gamma_l^d)^{0.5} (\gamma_s^d)^{0.5} + K, \quad (2)$$

where  $a$  is the cross-sectional area of solute,  $N$  is Avogadro's number,  $\gamma_l^d$  is the dispersive surface free energy of a solute, and  $K$  is a constant which depends on gas pressure and surface pressure. A linear plot can be obtained when (2) is fitted to n-alkane data. From the slope of this linear plot the dispersive component of the surface free energy,  $\gamma_s^d$ , can be evaluated. The  $a(\gamma_l^d)^{0.5}$  values for n-alkanes and for polar solutes are given in (Table 1). The free energy of adsorption,  $\Delta G_a$ , is related to the net retention volume as follows:

$$\Delta G_a = -RT \ln V_N + K. \quad (3)$$

The free energy of adsorption contains two components, namely, the specific component,  $\Delta G_a^S$ , and the dispersive component,  $\Delta G_a^d$ . Thus

$$\Delta G_a = \Delta G_a^d + \Delta G_a^S. \quad (4)$$

It is considered that the n-alkanes represent only dispersive interactions and polar solutes exhibit both dispersive and specific interactions. The  $\Delta G_a^S$  for polar solutes can be determined using a Fawkes plot and with help of the following relation:

$$\Delta G_a^S = RT \ln V_N - RT \ln V_N(\text{ref}), \quad (5)$$

where  $V_N$  is the net retention volume for a solute and  $V_N(\text{ref})$  is the net retention volume established by the n-alkane reference line for the same polar probe. For example the graphical evaluation of  $\Delta G_a^S$  has been shown in Figure 1 for dichloromethane at 323.15 K.

By determining the specific component of the surface free energy of adsorption at different temperatures, it is possible to compute the specific components of the enthalpy of adsorption,  $\Delta H_a^S$ , and entropy of adsorption,  $\Delta S_a^S$ , according to the following relation:

$$\frac{\Delta G_a^S}{T} = \frac{\Delta H_a^S}{T} - \Delta S_a^S. \quad (6)$$

The  $\Delta H_a^S$  values can be used to calculate the Lewis acidity parameter,  $K_a$ , and Lewis basicity parameter,  $K_b$ , using the following relation:

$$\frac{-\Delta H_a^S}{AN^*} = K_a \left( \frac{DN}{AN^*} \right) + K_b, \quad (7)$$

where  $AN^*$  and  $DN$  are Guttmann's modified acceptor and donor numbers, respectively. The  $AN^*$  and  $DN$  values of the polar solutes are included in Table 1.

TABLE 1: The properties of the solutes.

Solute	$a(\gamma_l^d)^{0.5} \times 10^{-16}$ $\text{cm}^2(\text{mJ}/\text{cm}^2)^{0.5}$	$a$ ( $\text{nm}^2$ )	$AN^*$ ( $\text{kJ}/\text{mol}$ )	$DN$ ( $\text{kJ}/\text{mol}$ )
n-Hexane	2.21	0.515	—	—
n-Heptane	2.57	0.570	—	—
n-Octane	2.91	0.630	—	—
n-Nonane	3.29	0.690	—	—
DCM	1.65	0.315	16.4	0
TCM	2.24	0.440	22.7	0
AC	1.73	0.425	10.5	71.4
EA	1.95	0.480	6.3	71.8
THF	2.13	0.450	2.1	84.4

\* Gutmann parameter.

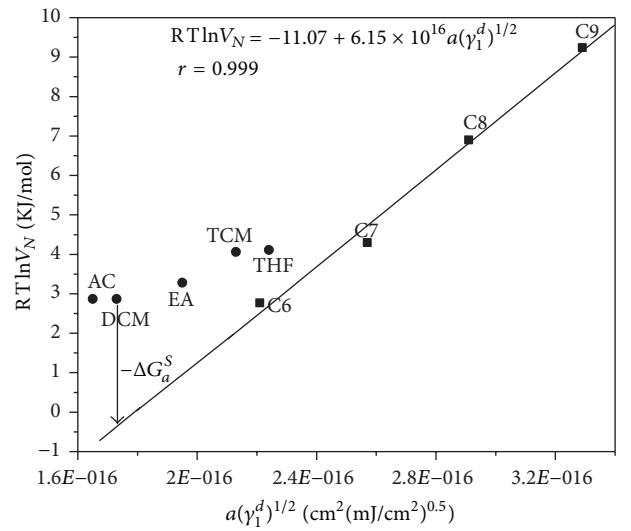


FIGURE 1:  $RT \ln V_N$  versus  $a\sqrt{\gamma_l^d}$  for n-alkanes and polar probes on PPA solid surface at 323.15 K.

### 3. Experimental

The retention times were measured using the dual column gas chromatograph and they were described earlier [7]. The PPA is purchased from Sigma-Aldrich in the granular form and it was used directly for column packing. A stainless steel column of 3 mm internal diameter and 30 cm length, obtained from NUCON, was cleaned with methanol and acetone and then dried in the oven. The column was packed with PPA particles directly with the aid of a mechanical vibrator. Both ends of the column were closely plugged with glass wool. One end of the column was fixed at the injector side and the other end was open at the detector side and equilibrated at room temperature for 12 hours under the flow of nitrogen carrier gas. The solutes n-alkanes, dichloromethane (DCM), trichloromethane (TCM), acetone (AC), ethyl acetate (EA), and tetrahydrofuran (THF) were analytical grade compounds purchased from S.D. Fine and Merck. 0.1  $\mu\text{L}$  of each solute was injected using a Hamilton syringe. The retention times were measured at constant oven temperature at intervals of 5°C in

TABLE 2: The values of  $RT \ln V_N$  (kJ/mol) for the n-alkanes and polar solutes on PPA drug in the temperature range 318.15–333.15 K.

Solute	318.15 K	323.15 K	328.15 K	333.15 K
n-Hexane	2.01	2.77	1.94	1.77
n-Heptane	3.62	4.3	2.92	2.47
n-Octane	6.88	6.9	4.07	2.99
n-Nonane	8.70	9.24	8.16	6.68
DCM	2.78	2.87	2.05	1.77
TCM	4.18	4.12	3.09	2.74
AC	2.2	2.87	2.16	1.91
THF	4.13	4.06	2.67	2.35
EA	4.39	3.28	2.48	2.24

the temperature range from 318.15 to 333.15 K. Each solute was injected three times and the average of the three retention times was used in the calculation of the net retention volume. The difference in the reproducibility of the retention time was less than 1 sec and this corresponds to an error of less than 1% in the evaluation of  $V_N$ .

#### 4. Results and Discussion

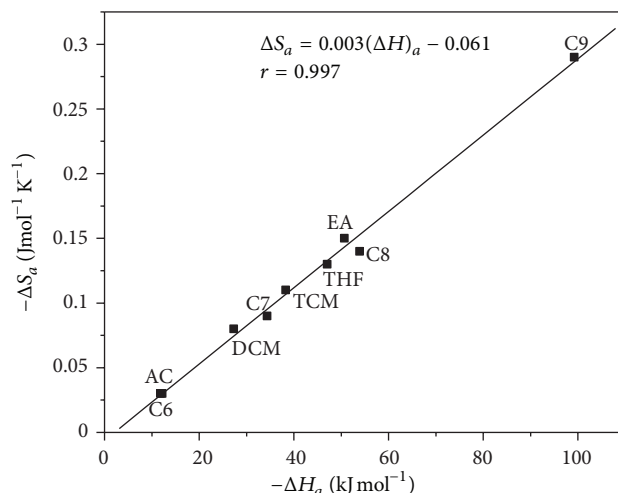
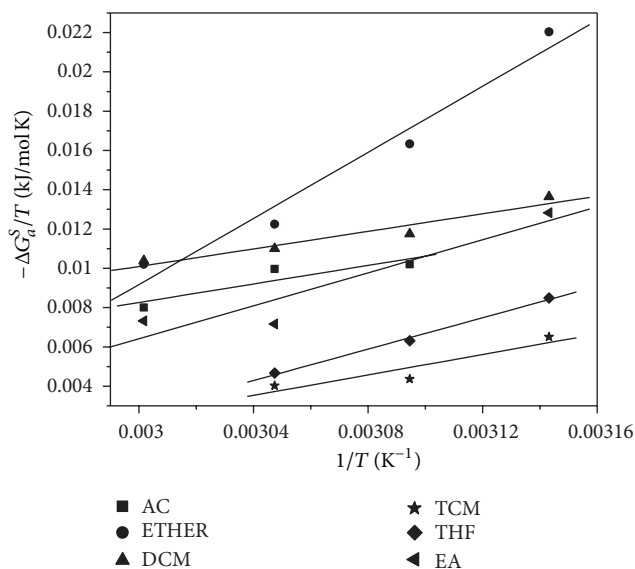
The values of  $RT \ln V_N$  for the n-alkanes and polar solutes at the four temperatures are given in Table 2. The  $RT \ln V_N$  values are maximum at 323.15 K and decrease with increase of temperature in the range 323.15 to 333.15 K. The dispersive surface free energy,  $\gamma_s^d$ , has been evaluated using (2). In the Schultz method, the  $\gamma_s^d$  has been calculated using the slope of the plot drawn between  $RT \ln V_N$  versus  $a(\gamma_l^d)^{0.5}$  for n-alkanes. Such plot has been shown in Figure 1 for the data measured at 323.15 K. A straight line plot is obtained for the n-alkane series and the points for polar probes are above the n-alkane reference line. The  $\gamma_s^d$  values of PPA are given in Table 3. It is observed that the  $\gamma_s^d$  values are decreased with increase of temperature and the temperature gradient is found to be  $-0.887 \pm 0.036 \text{ mJ m}^{-2} \text{ K}^{-1}$ . The free energy of adsorption,  $\Delta G_a$ , for the adsorption of solutes on PPA drug surface has been calculated using (3). Following (6), a linear fit between  $-\Delta G_a/T$  and  $1/T$  for n-alkanes and polar solutes gave negative enthalpy of adsorption,  $\Delta H_a$ , and entropy of adsorption,  $\Delta S_a$ . Both  $\Delta H_a$  and  $\Delta S_a$  are negative and a correlation between  $-\Delta H_a$  and  $-\Delta S_a$  has been shown in Figure 2 with correlation coefficient 0.997. The interaction intensity between PPA and the solute probe is a measure of the enthalpy of adsorption. If  $\Delta H_a$  is more negative, then the interaction will be considered as stronger. For the n-alkane series the  $-\Delta H_a$  is in the following order:

$$\text{n-hexane} < \text{n-heptane} < \text{n-octane} < \text{n-nonane}. \quad (8)$$

Further, the entropy of adsorption,  $\Delta S_a$  is also negative for all the n-alkanes. It is expected since the solute goes from the less ordered vapor phase to the more ordered adsorbed phase.

TABLE 3: Dispersive surface free energy,  $\gamma_s^d$ , of PPA surface in the temperature range 318.15–333.15 K.

T/K	318.15 K	323.15 K	328.15 K	333.15 K
$\gamma_s^d \text{ (mJ m}^{-2}\text{)}$	$26.63 \pm 3.86$	$26.01 \pm 0.40$	$21.90 \pm 5.25$	$17.14 \pm 4.79$

FIGURE 2: The correlation between entropy of adsorption,  $\Delta S_a$ , and enthalpy of adsorption,  $\Delta H_a$ , or solutes of PPA.FIGURE 3: The plot of  $-\Delta G_a^S/T$  versus  $1/T$  on PPA drug.

The specific component of free energy of adsorption,  $\Delta G_a^S$ , is calculated using (5) and the values are given in Table 4. The  $\Delta G_a^S$  values are negative for all the solutes. The linear fit between  $-\Delta G_a^S/T$  versus  $1/T$  shown in Figure 3 for the five polar solutes gave the specific enthalpy of adsorption,  $\Delta H_a^S$ , and specific entropy of adsorption,  $\Delta S_a^S$ . The  $\Delta H_a^S$  and  $\Delta S_a^S$  values are negative and are given in (Table 5). The  $\Delta H_a^S$  values

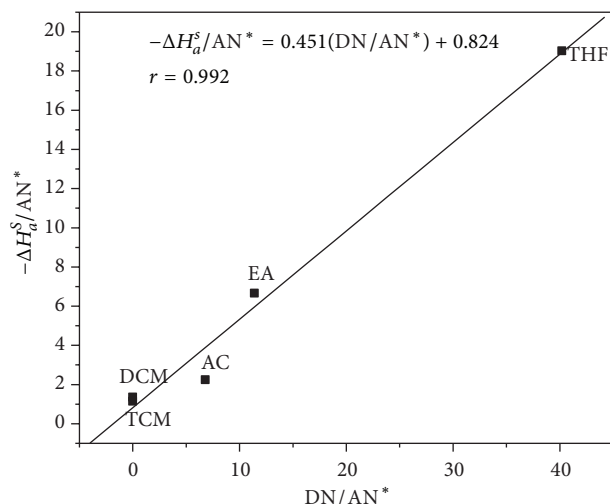


FIGURE 4: Plot of  $-\Delta H_a^S/AN^*$  versus  $DN/AN^*$  for the surface of PPA.

TABLE 4: The specific component of the surface free energy  $-\Delta G_a^S$  (kJ/mol) for polar solutes on PPA.

Solute	318.15 K	323.15 K	328.15 K	333.15 K
DCM	4.43	3.80	3.61	3.46
TCM	2.07	1.41	1.32	1.50
AC	3.26	3.31	3.27	3.21
THF	2.70	2.04	1.53	1.65
EA	4.08	2.36	2.35	2.44

TABLE 5: The specific components of the enthalpy of adsorption,  $\Delta H_a^S$ , entropy of adsorption,  $\Delta S_a^S$ , and correlation coefficient,  $r$ , for polar probes on PPA.

Solute	$-\Delta H_a^S$ (kJ/mol)	$-\Delta S_a^S$ (kJ/mol K)	$r$
DCM	$22.37 \pm 4.33$	$0.057 \pm 0.01$	0.965
TCM	$26.03 \pm 10.37$	$0.076 \pm 0.03$	0.925
AC	$23.59 \pm 10.96$	$0.063 \pm 0.03$	0.907
EA	$41.97 \pm 15.19$	$0.119 \pm 0.05$	0.940
THF	$39.95 \pm 2.83$	$0.117 \pm 0.09$	0.998

along with Guttmann parameters of polar solutes are used to evaluate the acid-base character of PPA surface. The Lewis acidity parameter,  $K_a$ , and basicity parameter,  $K_b$ , can be obtained from the slope and intercept of (7). Therefore, a plot was drawn between  $-\Delta H_a^S/AN^*$  versus  $DN/AN^*$  in Figure 4, which is found to be linear with correlation coefficient,  $r = 0.992$ . The  $K_a$  and  $K_b$  values are  $0.451 \pm 0.033$  and  $0.824 \pm 0.622$ , respectively, which suggest that the PPA surface contains more basic sites and less number of acidic sites. The  $-\text{OH}$  and  $\text{NH}_2$  functional groups in the structure of PPA are responding for the acidic and basic sites on the surface of PPA. The  $K_a$  and  $K_b$  values indicate that the  $\text{NH}_2$  groups dominate on the surface of PPA. Further if the ratio  $K_b/K_a$  is greater than unity, then the overall character of the surface is basic. In the PPA the ratio is 1.83 which conveys that the drug

surface is basic in character and interacts strongly with acidic environment.

## 5. Conclusion

The  $V_N$  values of n-alkanes and polar solutes on PPA solid surface are determined at four temperatures in the range from 318.15 to 333.15 K by IGC. The  $V_N$  values have been used to calculate the dispersive surface free energy and the Lewis acid-base parameters. The  $\gamma_s^d$  values are decreasing with increase of temperature and the value of  $\gamma_s^d$  at 323.15 K was found to be  $26.01 \text{ (mJ/m}^2\text{)}$ , respectively. Lewis acidity parameter,  $K_a$ , and Lewis basicity parameter,  $K_b$ , revealed that the PPA surface is more basic and less acidic. Hence, it may be concluded that PPA drug interact strongly with the acidic environment.

## Acknowledgment

B. Praveen Kumar is grateful to the University Grants Commission, Basic Scientific Research (UGC-BSR), New Delhi, for the award of Meritorious Research Fellowship.

## References

- [1] M. R. Sunkersett, I. M. Grimsey, S. W. Doughty, J. C. Osborn, P. York, and R. C. Rowe, "The changes in surface energetics with relative humidity of carbamazepine and paracetamol as measured by inverse gas chromatography," *European Journal of Pharmaceutical Sciences*, vol. 13, no. 2, pp. 219–225, 2001.
- [2] V. Swaminathan, J. Cobb, and I. Saracovan, "Measurement of the surface energy of lubricated pharmaceutical powders by inverse gas chromatography," *International Journal of Pharmaceutics*, vol. 312, no. 1-2, pp. 158–165, 2006.
- [3] F. Thielmann, "Introduction into the characterisation of porous materials by inverse gas chromatography," *Journal of Chromatography A*, vol. 1037, no. 1-2, pp. 115–123, 2004.
- [4] S. C. Das, Q. Zhou, D. A. V. Morton, I. Larson, and P. J. Stewart, "Use of surface energy distributions by inverse gas

- chromatography to understand mechanofusion processing and functionality of lactose coated with magnesium stearate,” *European Journal of Pharmaceutical Sciences*, vol. 43, no. 4, pp. 325–333, 2011.
- [5] P. Reddi Rani, S. Ramanaiah, B. Praveen Kumar, and K. S. Reddy, “Lewis acid-base properties of cellulose acetate butyrate-poly (caprolactone diol) blend by inverse gas chromatography,” *Polymer-Plastics Technology and Engineering*, vol. 50, pp. 1–7, 2011.
- [6] A. Al-Ghamdi, M. Melibari, and Z. Y. Al-Saigh, “Characterization of biodegradable polymers by inverse gas chromatography. II. blends of amylopectin and poly( $\epsilon$ -caprolactone),” *Journal of Applied Polymer Science*, vol. 101, no. 5, pp. 3076–3089, 2006.
- [7] T. V. M. Sreekanth, S. Ramanaiah, P. Reddi Rani, and K. S. Reddy, “Thermodynamic characterization of poly (caprolactone-diol) by inverse gas chromatography,” *Polymer Bulletin*, vol. 63, no. 4, pp. 547–563, 2009.
- [8] M. D. Jones, P. Young, and D. Traini, “The use of inverse gas chromatography for the study of lactose and pharmaceutical materials used in dry powder inhalers,” *Advanced Drug Delivery Reviews*, vol. 64, no. 3, pp. 285–293, 2012.
- [9] J. Patera, P. Zamostny, D. Litva, Z. Berova, and Z. Belohlav, “Evaluation of functional characteristics of lactose by inverse gas chromatography,” *Procedia Engineering*, vol. 42, pp. 707–715, 2012.
- [10] P. Mukhopadhyay and H. P. Schreiber, “Aspects of acid-base interactions and use of inverse gas chromatography,” *Colloids and Surfaces A*, vol. 100, pp. 47–71, 1995.
- [11] T. Hamieh, M.-B. Fadlallah, and J. Schultz, “New approach to characterise physicochemical properties of solid substrates by inverse gas chromatography at infinite dilution—III. Determination of the acid-base properties of some solid substrates (polymers, oxides and carbon fibres): a new model,” *Journal of Chromatography A*, vol. 969, no. 1-2, pp. 37–47, 2002.
- [12] M. Kunaver, J. Zadnik, O. Planinšek, and S. Srčič, “Inverse gas chromatography—a different approach to characterization of solids and liquids,” *Acta Chimica Slovenica*, vol. 51, no. 3, pp. 373–394, 2004.
- [13] J. M. R. C. A. Santos and J. T. Guthrie, “Analysis of interactions in multicomponent polymeric systems: the key-role of inverse gas chromatography,” *Materials Science and Engineering R*, vol. 50, no. 3, pp. 79–107, 2005.
- [14] A. Voelkel, B. Strzemiescka, K. Adamska, and K. Milczewska, “Inverse gas chromatography as a source of physiochemical data,” *Journal of Chromatography A*, vol. 1216, no. 10, pp. 1551–1566, 2009.
- [15] J. Schultz, L. Lavielle, and C. Martin, “The role of the interface in carbon fibre-epoxy composites,” *Journal of Adhesion*, vol. 23, pp. 45–60, 1987.



