The first right hand term of Eqs. 7 and 10 express London interaction (dispersion forces) between solute and solvent. These omnidirectional forces do not operate only on 67% of the nearest neighbor molecules, as suggested by the coefficient of Eq. 7, nor on 74%, as shown in Eq. 10. Instead, the coefficient of the $(\delta_{1d} - \delta_{2d})^2$ term should be unity. This can be ensured in the regression method by moving this term to the left hand side of the expression for the calculation of coefficients, then returning it to the right side to display the final equation. The δ_{2d} was taken as 9.40 and the equation obtained was:

$$(\log\alpha_2)/A = (\delta_{1d} - 9.40)^2 - 0.1463(\delta_{1p} - 2.059)^2 + 0.1319(\delta_{1h} - 0.778)^2 + 0.8640 \quad \text{(Eq. 12)}$$

This method reduces the variables of regression by one, but it does not seriously reduce the correlation coefficient: R^2 of Eq. 7 is 0.986 and of Eq. 12 is 0.980. Also from Eq. 13, $\delta_T{}^2 = 9.42 + 2.059^2 + 0.7782$; $\delta_T = (93.205)^{1/2} = 9.65$.

Although this report is devoted to the calculation of solubility parameters for crystalline solids, Eqs. 7, 10, and 12 provide the calculation of the solubility of naphthalene in both polar and nonpolar solvents, as was demonstrated in an earlier report (1). The results, $X_{2(calc)}$, are found in Table I together with the percentage error for naphthalene solubility in each of the 26 solvents studied. Most of the solubilities were very satisfactory, ~50% exhibiting errors of <10%. Most values have an error of < ~30%. Isopropanol and acetic acid exhibited errors of >30% when Eqs. 7 and 12 were used. The predicted solubilities for naphthalene in hexane, acetic acid, ethanol, methanol, and water were >30% error using Eq. 10. The reason that solubilities in these five solvents are >30% cannot be stated definitively at this time. Ethanol, methanol, isopropanol, acetic acid, and water are highly hydrogen bonded and exhibit self-association. However, other polar solvents such as propanol, butanol, and cyclohexanol have reasonable values in this work. The error of 37% for hexane is surprising, as this solvent tends to form regular solutions with nonpolar solutes such as naphthalene.

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GLC Determination of Phenacemide in Tablets

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Abstract □ A GLC procedure was developed for phenacemide and was shown to be less time consuming than the official assay without sacrificing accuracy. The procedure involves extraction from powdered tablets and addition of pentylenetetrazol as the internal standard. The amount of phenacemide is determined by comparison of the ratio of the area under the curves to that of a standard.

Keyphrases □ Phenacemide—analysis in tablets, GLC determination, pentylenetetrazol □ Pentylenetetrazol—analysis of phenacemide in tablets, GLC determination □ GLC—phenacemide, analysis in tablets, pentylenetetrazol.

Phenacemide, an open chain analog of 5-phenylhydantoin, is used in temporal lobe epilepsy (psychomotor) which is refractory to other agents (1, 2). It is a white, odorless, and tasteless crystalline solid (3). While performing routine analyses in another experiment, a rapid method of analysis for phenacemide was needed. The official assay involves acid hydrolysis, extraction of the acidic products into chloroform, and back titration (4). The procedure is time consuming and requires much handling and transfer. Other methods for phenacemide determination have been developed but offer no distinct advantages (5–7).

This report outlines a rapid GLC method that has proven to be less time consuming. In addition to requiring less handling and transfer, it does not appear to sacrifice accuracy.

EXPERIMENTAL

Materials—Phenacemide powder[1] and phenacemide tablets[1] were utilized in the assay as received. Pentylenetetrazol[2] was used as the internal standard. Methanol[3] and isopropyl alcohol[3], ACS reagent grade, were used as solvents.

Apparatus—A basic gas chromatograph[4] with a flame ionization detector (FID) was used. A 3.17-mm, 1.83-m silicone column[5] was used. The temperature of the column and detector was maintained at 200 ± 20°. The flow rate of the carrier gas (helium) was ~20 ml/min. The detector was connected to an integrating recorder[6] for easy and accurate determination of area under the curve.

Standard Curve—Seven samples of varying ratios of phenacemide to pentylenetetrazol in methanol (Table I) were used to obtain a standard curve. Exact amounts of phenacemide and pentylenetetrazol were weighed directly into 10-ml volumetric flasks. A small volume of methanol was added to dissolve the sample and then made to volume with methanol.

Three microliters of each of the seven solutions was chromatographed and the results recorded. A standard curve was obtained by plotting the

[1] Abbott Laboratories, North Chicago, IL 60064.
[2] Knoll Pharmaceutical, Whippany, NJ 07981.
[3] Fisher Scientific, Norcross, GA 30091.
[4] Model 9500, Carle Instruments, Fullerton, CA 92631.
[5] 8% G.E. SF96 Carle Instruments, Fullerton, CA 92631.
[6] Model 1005, Beckman Instruments, Fullerton, CA 92631.

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Table I—Samples Used to Construct the Standard Curve

Sample Number	Phenacemide, g/10 ml	Pentylenetetrazol, g/10 ml
1	0.0405	0.0215
2	0.0133	0.0501
3	0.0308	0.0535
4	0.0320	0.0399
5	0.0507	0.0506
6	0.0200	0.0520
7	0.0377	0.0305

ratio of the area under the curve of phenacemide to pentylenetetrazol *versus* the ratio of the concentration of phenacemide to pentylenetetrazol in moles per liter.

Analysis of Phenacemide—In keeping with the USP method, 20 tablets were crushed in a porcelain mortar and pestle. The powder was dried over anhydrous calcium sulfate[7] in a dessicator. Samples containing ~400 mg of drug were accurately weighed and placed in a 500-ml round bottom flask. Approximately 450 ml of isopropyl alcohol was added and the solution was refluxed for 1 hr, cooled to room temperature, and filtered. Approximately 500 mg of an accurately weighed sample of pentylenetetrazol was added and the solution was brought to volume (1 liter) with isopropyl alcohol. A 3-μl sample was injected onto the chromatograph and the area under the curve recorded. The average of at least three determinations was used in the subsequent calculations.

RESULTS AND DISCUSSION

The equation of the standard curve using regression analysis[8] was found to be:

$$y = 1.30x - 0.0612 \qquad \text{(Eq. 1)}$$

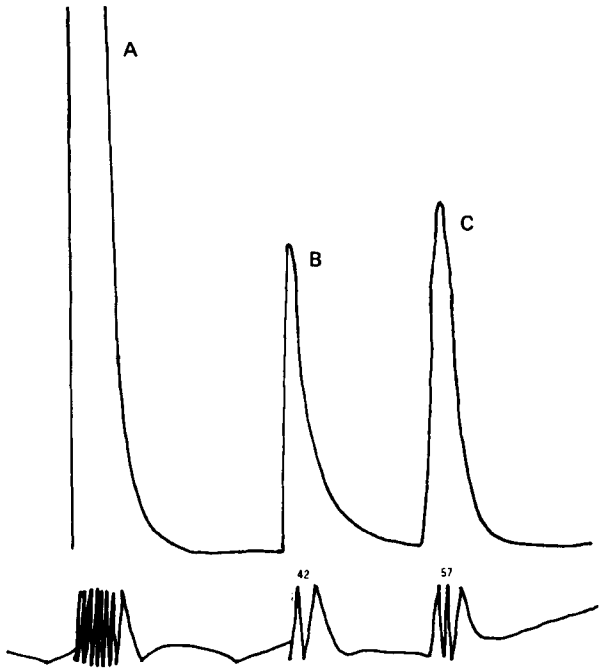

Figure 1—*A sample chromatogram from phenacemide tablets. Key: (A) solvent isopropyl alcohol; (B) phenacemide; (C) pentylenetetrazol.*

[7] Hammond Drierite Co., Xenia, OH 45385.
[8] Statistical Analysis System, SAS Institute, Raleigh, NC 27605.

Table II—Recovery and Assay Results from USP and GLC Methods

Phenacemide[a], g	Expected Phenacemide Control, g	Phenacemide Found, g	Recovery, %
	GLC Method		
0.5726	0.3843	0.3985	103.8
0.5966	0.4004	0.4120	102.9
0.5946	0.3991	0.4152	104.0
0.5950	0.3993	0.3993	100.1
	USP Method		
0.5944	0.4002	0.3976	99.4
0.5969	0.4006	0.4148	100.6
0.5962	0.4002	0.3992	99.8

[a] Powdered tablet weighed.

where:

$$y = \frac{\text{area under the curve of phenacemide}}{\text{area under the curve of pentylenetetrazol}} = \frac{AUCP}{AUCM} \qquad \text{(Eq. 2)}$$

$$= \frac{\text{concentration of phenacemide}}{\text{concentration of pentylenetetrazol}} = \frac{CONCP}{CONCM} \qquad \text{(Eq. 3)}$$

The standard curve was linear and the amount of phenacemide was determined using Eq. 1. The values are recorded in Table II.

The gas chromatogram resulting from each sample injection exhibited three peaks: the solvent (isopropyl alcohol), phenacemide, and pentylenetetrazol. Tailing was minimal and each peak approached the base line before the appearance of the next peak. A typical chromatogram is shown in Fig. 1.

The standard curve was linear in the range used for this study. The correlation coefficient of concentration *versus* area under the curve was 0.9996. Statistical comparison, using Student's t test for independent samples, showed no statistical difference between recovery of phenacemide using the USP assay and the GLC method. The calculated t-value was 0.7649, while the critical value was $t_{0.95} = 2.571$, with 5 df.

The GLC determination of phenacemide in tablets offers an improvement over the USP method without sacrificing accuracy in the samples assayed. The GLC determination of phenacemide in tablets is a simpler and quicker method which produces results essentially the same as that of the time-consuming official assay.

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