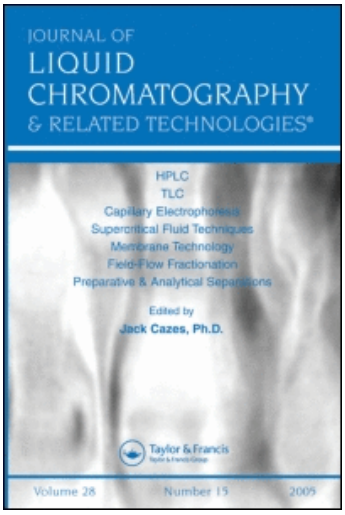

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Use of HPLC to Estimate Solubility Parameters of Impurities

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USE OF HPLC TO ESTIMATE SOLUBILITY PARAMETERS OF IMPURITIES

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ABSTRACT

The chromatographic retention time was found to vary with the solubility parameter of the eluting component of known structure. A linear relationship was obtained between the retention times and calculated solubility parameters of the species used in this study. This correlation was used to estimate the solubility parameters of the extra peaks appeared in the chromatogram presumably the impurities present in the components.

INTRODUCTION

The solubility parameter is one of the most useful concept in polymer science to predict solvent, swelling agents and nonsolvents for a polymeric material[1,2]. Commutation of solubility parameter of structurally known components from the cohesive energy density by group addition method is certainly an easier task. Fortunately through the efforts of Small, Hoy, Fedors, Van krevelen and many others, cohesive energy density is available for almost all groups[2,3,4,5]. However, estimation of solubility parameter of an unknown components like impurities present in a given chemical is relatively a tougher job. This

note attempts to use HPLC to determine the solubility parameter from chromatographic retention data.

EXPERIMENTAL

Phthalate esters Di(2-ethylhexyl)phthalate (DEHP), Dibutyl phthalate (DBP), Diethylphthalate (DEP) and Di methyl phthalate (DMP) were from Indo-Nippon Co., Bombay. Hatcol-200 (Hatco Co NJ) was a generous gift from Mr. K. Rathinam. All other reagents were analytical grade or spectroscopic grade and used an received except chloroform which was distilled prior to use.

Chromatographic system employed consisted of a Waters Assoc. Inc. Model 6000 A solvent delivery pump, 440 absorbance detector and U6K injector. For separating the components a μ-Porasil column was used. Details of mobile phase compositions used in this study are summarized in Table-1. The components were dissolved in the appropriate mobile phases and injected onto the column. The peaks were monitored at 254 nm and the chromatograms were obtained on an ominiscribe recorder (Houston Instruments Tx).

The solubility parameters were estimated by the equation $\sum_i (E_i/V_i)^{\frac{1}{2}}$ where E_i is the cohesive energy of each group and V_i is the respective molar volume. The value, reported in the literature were used for the calculation[2].

RESULTS AND DISCUSSION

Fig.1 depicts a typical chromatogram of the plasticizers. The single solubility parameter computed for these components by group addition method, mobile phase composition and subsequent retention time are summarized in Table 1. Log t (retention

TABLE-I

CHROMATOGRAPHIC CONDITIONS AND SOLUBILITY PARAMETERS (CALCULATED) OF THE COMPONENTS USED

Mobile Phase	Retention Time (min)					Solubility Parameter $(J/cm^3)^{\frac{1}{2}}$
	DMP	DEP	DBP	DOP	HATCOL-200	
n-hexane: chloroform (65:35 v/v)	10.1	8.9	7.2	6.1	5.2	19.7 (Hatcol-200)
Carbon tetrachloride: Methylene chloride (60:40 v/v)	7.4	6.8	5.8	5.3	5	23.53 (DMP) 22.58 (DEP) 21.36 (DBP)
Chloroform: glacial Acetic Acid (95:10 v/v)	6.2	5.8	5.4	5.1	4.8	20.12 (DOP)

time) versus solubility parameter (δ) was linear irrespective of mobile phases and a representative plot is shown in Fig.2. The plot can be expressed by a simple relation $\log t = a+b$ where a and b are constants depending upon the chromatographic conditions.

A knowledge on the solubility characteristics of impurities if any present in a polymer additive intended for biomedical grade polymeric formulation is necessary to know the dissolution of the impurities to body fluids. Solubility parameter can reflect hydrophilic/hydrophobic nature of a component.

Polymers containing different additives have been used for varied medical applications. Polyvinyl chloride (PVC) is perhaps the most videly used polymer for disposable medical uses[6].

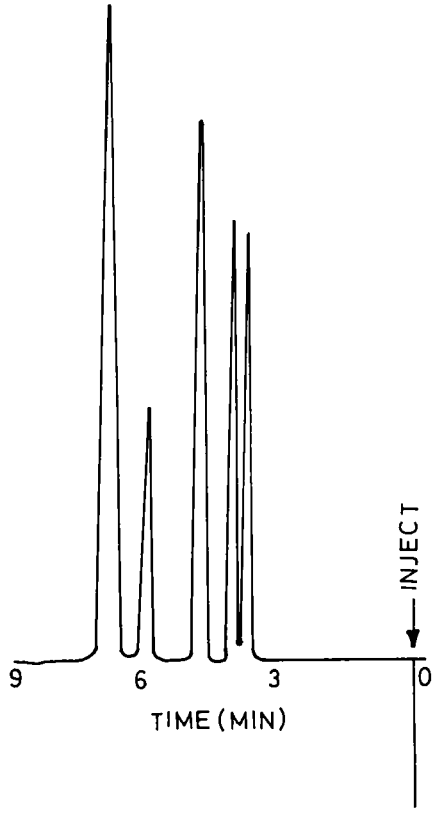

FIG.1 : A typical chromatogram of plasticizers. Mobile phase Glacial Acetic Acid: Chloroform (10:95 v/v). Peaks: 1-Hatcol-200, 2-DOP, 3-DBP, 4-DEP and 5-DMP.

PVC formulation intended for medical application consists several additives among which DEHP is the major one. Since the toxic liabilities may arise from the impurities present in these additives, intensive quality assay is normally performed particularly when a fresh batch of additive is received. Fig.3 is a chromatogram of a commercial sample of DEHP. The chromatogram

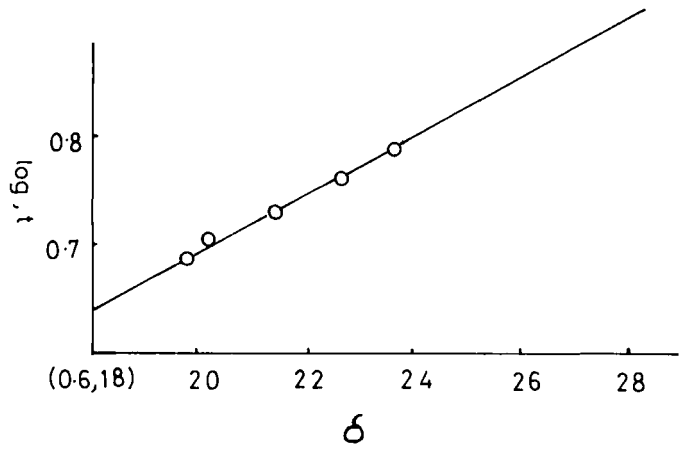

FIG.2 : A plot of log t vs solubility parameter.

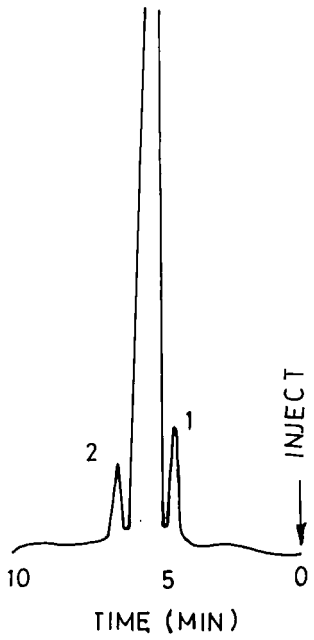

FIG.3 : Chromatogram of a commercial sample of DEHP. Mobile phase chloroform: glacial acetic acid (95:10 v/v).

shows that this sample contain two extra components (Peak 1 and 2) corresponding to a retention time of 5 and 5.3 min. respectively. The solubility parameter of these components were estimated from log t - δ plot. The values obtained for these two components were 20.2 $(J/cm^3)^{\frac{1}{2}}$ (Peak 1) and 21 $(J/cm^3)^{\frac{1}{2}}$ (Peak 2). Based on these values the leachability of these extra components to body fluids would be peak 2 > DEHP > peak 1. i.e. the solubility of one of the impurity (Peak 2) would be more than that of the DEHP.

Blood stored in PVC containers for nearly one month was subjected to Chromatographic analysis to estimate the leached out plasticizer after the extraction procedures as reported earlier[7]. The mobile phase was chloroform glacial acetic acid (95:10 v/v). We observed DEHP as well as an additional peak at 6.1 min. which corresponds to a solubility parameter of 23.2 $(J/cm^3)^{\frac{1}{2}}$. Subsequently this peak was identified as mono(2-ethyl hexyl)phthalate (MEHP). The close agreement of calculated solubility parameter (22.74$(J/cm^3)^{\frac{1}{2}}$ and the value obtained from graph (23.2) indicates the feasibility of the method for estimating solubility parameter. These two examples cited, apparently indicate the applicability of the method at least in a limited way. Normally, for any additive, a chromatographic purity assay is performed. The present method enables to estimate the solubility parameter of any extra peaks of the probable contaminents, from the simple chromatogram.

The ability of HPLC to provide physical chemical parameters has been well recognized[8,9]. HPLC procedures now almost replaced the classical shake flask method for estimating the partition coefficient[10,11,12]. HPLC methodologies have been employed routine-

ly to understand a variety of parameters like LD_{50}, partition coefficient, ionisation constants etc.[12,13,14]. Among these diversified applications, the present method is perhaps the first of this kind to estimate solubility parameter. The serious drawback of the method is its incompatibility with gradient elution. The merits of the method can be assessed only by analysing and correlating wide and varied classes of components. However, the limited data reported here suggests that it would be used to estimate the solubility parameter of impurities present, at least in a homologous series.

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