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ACKNOWLEDGMENTS AND ADDRESSES

Received May 22, 1968, from the *Department of Pharmaceutical Analytical Chemistry, University of Kansas, Lawrence, KS 66044 (T.H.)* and *School of Pharmacy, University of Wisconsin, Madison, WI 53706 (A.F.M.)*

Accepted for publication October 7, 1968.

Presented before the Drug Standards, Analysis and Control Section, APhA Academy of Pharmaceutical Sciences, Miami Beach meeting, May 1968.

This study was supported in part by grants from the Roche Laboratories of Nutley, N. J., and Smith, Kline & French Laboratories, Philadelphia, Pa.

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Solubility of the Parabens in Dioxane–Water Mixtures

ANTHONY N. PARUTA

Abstract ☐ The solubilities of methyl, ethyl, propyl, and butyl parabens have been determined in aqueous solutions of dioxane at 25°. A dielectric requirement of about 8–10 was found for the above materials. Two-phase systems were found for the ethyl, propyl, and butyl derivatives over a given composition range for the binary mixture. Phase separation occurred over a broad range of composition for the butyl derivative, intermediate range for propyl, and a narrow range for the ethyl derivative. The two phases were found to be invariant with respect to the concentration of the components of the ternary system. It is suggested that a solvate between the paraben and a fixed composition of the binary mixture is produced forming a biphasic system in equilibrium.

Keyphrases ☐ Parabens solubility—dioxane-water mixtures ☐ Dielectric requirements—parabens solubility ☐ Dielectric constants—dioxane-water mixtures ☐ UV spectrophotometry—analysis

The solubility behavior of parabens has been previously reported (1–3) in sucrose solutions and a wide spectrum of pure alcohols. The solubility parameter value for these compounds was found to be about 11.0 by Martin (2). It was also shown that these compounds possessed dielectric requirements (DR) of 14 and possibly another at a dielectric constant of 30 (3). It was thought instructive that solubility studies should be conducted on these compounds over a wide range of dielectric constants produced by a given binary system. Since dioxane-water mixtures encompass the above DR's possessing a dielectric constant span of values from 2 to about 80, this system was chosen. It was expected that a twin-peak array should be evidenced for the solubility profile having approximate DR values of 14 and 30.

It was further hoped that some sort of delineation of the effect of substituent groups could be found in either the nature of the solubility curves or in the magnitude of the solubility for these compounds.

EXPERIMENTAL

Reagents—Methyl, ethyl, propyl, and butyl parabens were used.[1] Dioxane (stabilized)[2] and distilled water were the solvents used All the reagents were used directly as no pretreatment of solutes was considered necessary.

Procedure—Solubilities were determined by a gravimetric procedure at 25 ± 0.1° maintained by a water bath as previously described (4). In the case of two liquid layers, samples were withdrawn from the upper layer first through a pipet fitted with a glass-wool pledget. The vial was tilted and another prepared pipet was quickly introduced into the lower layer and a sample withdrawn. Each prarben was subjected to three solubility runs and average results are given. Several samples of the two liquid systems formed were also checked by analyzing by spectrophotometric means[3] at 255 mμ.

RESULTS AND DISCUSSION

In Fig. 1, the solubility of both methyl and ethyl paraben are shown in mg./ml. as a function of the dielectric constants of the binary mixtures. A definite solubility maximum occurs at a dielectric constant value of 10 for both these compounds. In the case of ethyl paraben, two liquid phases are formed over a dielectric

[1] Methyl (No. 5266), ethyl (No. 5082), propyl (No. 5294), butyl (No. 5158), Matheson, Coleman and Bell, East Rutherford, N. J.
[2] No. 4937, Mallinckrodt, St. Louis, Mo.
[3] Cary model 16 spectrophotometer.

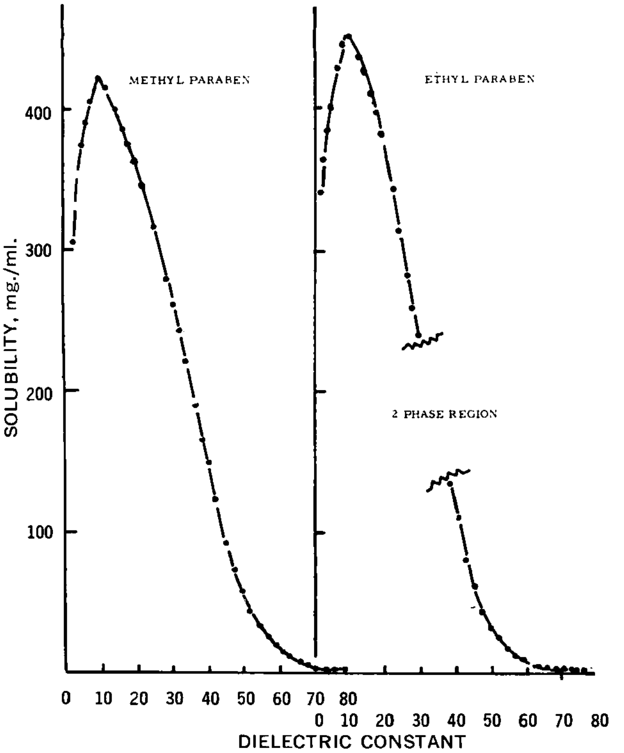

Figure 1—*A plot of the solubility at 25° in mg./ml. for methyl and ethyl paraben as a function of the dielectric constant of the binary solvents.*

constant range of 31–37 which could not be analyzed conveniently. Introduction of a pipet into these samples caused immediate precipitation and the sample became a very viscous slurry. The dielectric requirement of 10 for this binary system of dioxane and water is fairly close to the value of 14 from the pure solvent scan (1). However, the expected shouldering at a dielectric constant value of 30 was not seen for the methyl compound. It is possible that the solubility in this dielectric constant range is changing so rapidly that this shoulder cannot be seen. In the case of ethyl paraben, the dielectric constant range around 30 produces a two-phase system, so it would be impossible to see a break. These solubility curves have been plotted on superimposed X-axis for convenience in observing the nature of these curves.

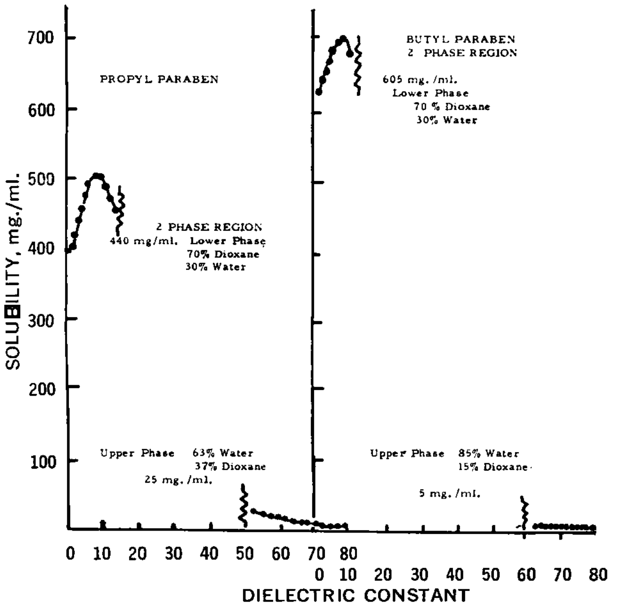

Figure 2—*This plot parallels Fig. 1 for propyl and butyl parabens.*

Table I—Composition of the Two Liquid Phases Formed for the Parabens in Equilibrium and the Dielectric Constant Range

		Concn. (w/w)					
		Upper Phase			Lower Phase		
Paraben	ε Range	Paraben	Dioxane	Water	Paraben	Dioxane	Water
Ethyl	31–37	13	44	43	24	53	23
Propyl	15–50	3	36	61	44	39	17
Butyl	11–60	0.5	15	84.5	60	28	12

The solubility of propyl and butyl parabens are shown in Fig. 2 in the same manner previously described. In the case of propyl paraben, a maximum is evidenced at a dielectric constant of 10 and a two-phase region over a relatively wide dielectric constant range. This range is seen to exist at values of 15 to 50, and the composition of the two phases formed are also shown. In the two-phase region, the composition was found to be invariant; however, the relative amounts of the two phases varied. The dioxane-rich phase was the lower denser phase, whereas the water-rich phase was the upper less dense phase. The composition of the lower dioxane-rich phase was propyl paraben 44.0, dioxane 39.2, and water 16.8, whereas the upper phase was found to be propyl paraben 2.5, dioxane, 36.0, and water 61.5. The solubility profile of butyl paraben also shows a maximum at a dielectric requirement of 10 and an even wider dielectric constant range for the formation of the two-phase region, *i.e.*, $\epsilon = 11$–60. It can be easily seen that in going from the methyl to the butyl derivative, the two-phase region increases over an ever widening range. Obviously, the DR of about 30 predicted earlier from the pure solvent scan cannot, under the aforementioned circumstances, be seen. The composition of the lower phase was found to be butyl paraben 60, dioxane 28, and water 12, whereas the upper phase was found to have butyl paraben 0.5, dioxane 15.4, and water 84.6. Assuming that the data for ethyl paraben could be handled in the same manner, the composition of upper and lower phases could be calculated. These results are summarized in Table I.

In Fig. 3, the solubility profiles for the parabens have been summarized over the polarity range where solutions are formed. This has been done with a view of comparing the magntiude of solubility for any given paraben to the methyl derivative. In other words, the effect of the added methylene group on the solubility at con-

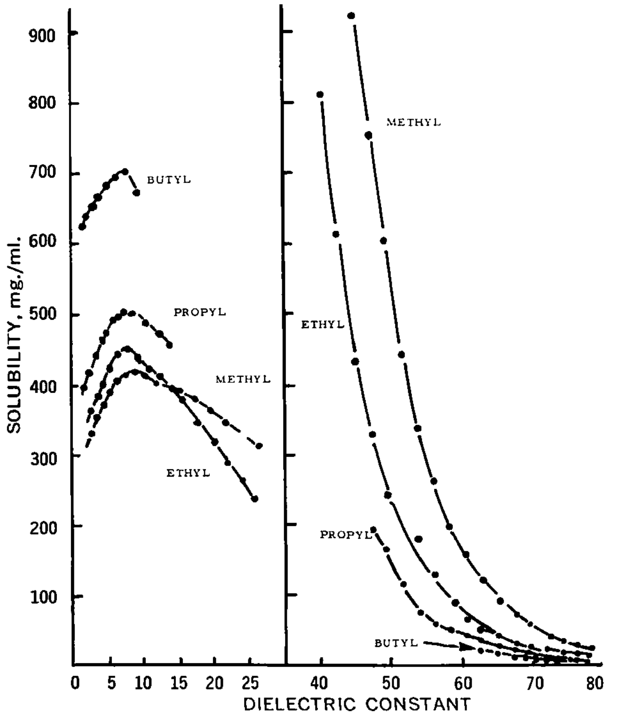

Figure 3—*A composite plot of the solubility at 25° in mg./ml. for the parabens rotes over a limited range of dielectric constants where solutions are formed.*

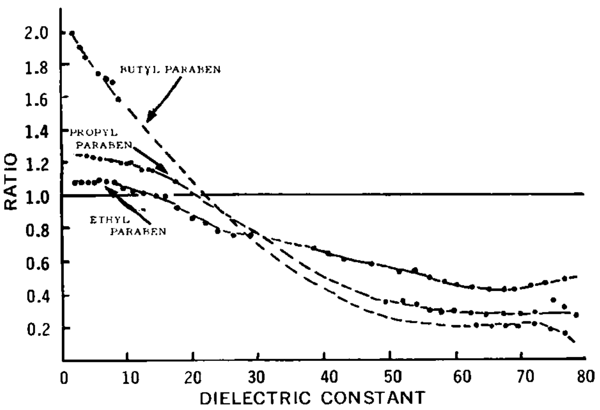

Figure 4—*A plot of the ratio of the solubility at 25° in mg./ml. for each paraben relative to methyl paraben at any given dielectric constant value.*

stant, polarity *i.e.*, the dielectric constant, was studied. Thus, the solubility profiles, although seemingly approximately parallel when seen in Fig. 3, are, in fact, not parallel. In Fig. 4, the solubility ratio is shown defining methyl paraben as unity. At lower dielectric constant values, the slopes of these ratios increase with increasing *n*-alkyl groups. On the other hand, at dielectric constant values of 45 or greater, implying moderate to high polarity, a fair degree of parallelism is observed. The dashed lines in this figure imply the probable value of the ratio were true solutions over that dielectric constant range formed.

In Fig. 5, the phase volume ratio of upper phase for the propyl and butyl parabens in these systems as a function of concentration is shown. It can be seen that the less dense water-rich upper phase increased in relative amount as the water concentration increased. The values shown for ethyl were calculated from the data and this compound has the largest slope, with the butyl derivative having the least slope. This indicates that the addition of increasing amounts of water changes the relative amount of the water-rich upper phase to a greater degree for the ethyl compound and the least degree for the butyl compound. The propyl derivative is intermediate in value.

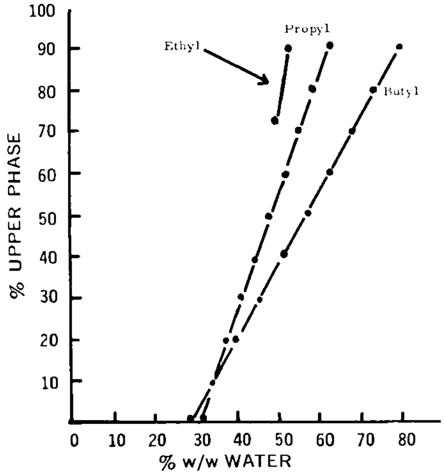

Figure 5—*A plot of the phase volume ratio in which the percent of upper phase is shown as a function of increasing water content.*

Table II—Number of Molecules of Each Component in the Two Liquid Phases for the Parabens in Dioxane-Water Mixtures

Paraben	Solute	Numbers of Molecules Dioxane (A)	Water (B)	B/A
		Upper Phase		
Ethyl	1	7	30	
Propyl	1	33	248	
Butyl	1	77	1,890	
		Lower Phase		
Ethyl	1	4.8	8.9	1.86
Propyl	1	2.0	3.9	1.95
Butyl	1	1.2	2.1	1.75

The invariant composition of the two liquid phases in equilibrium with each other was examined relative to the molecular ratio of the three components. The numbers of molecules of the solvents in the binary mixture associated with one molecule of "solute" have been calculated and are shown in Table II.

As can be seen from Table II, there is a recurrence of a constant value relative to the content of the solvents for the lower phase.

Since the solvents are in a basic ratio of 1:2 for dioxane to water, it is possible that this is the type of solvate formed for the materials. It would seem that the difference in these compounds is simply the number of times this solvate unit occurs. Thus, the approximate formula for these materials could be written as ethyl paraben (1 dioxane·2 water)$_5$, propyl paraben (1 dioxane·2 water)$_2$, and butyl paraben (1 dioxane·2 water)$_1$.

No relationship of the above type could be found for the upper phase as would be expected since the relative value of solubility for these parabens would cause them not to contribute significantly to its overall concentration.

SUMMARY

It has been found that the parabens in this study possess a DR of about 10 which correlates only to a fair degree with a value of 14 from the pure solvent scan. Two liquid phases in equilibrium with each other were found to exist for ethyl, propyl, and the butyl derivative over an ever increasing dielectric constant range in the stated order. These liquid phases were found to be invariant with respect to the concentration of the components. Calculations based on the numbers of molecules of each component in the lower phase show and may indicate a solvate is formed having a ratio of dioxane to water of 1:2.

Another study on the solubility characteristics is presently underway and will be the subject of future communications.

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ACKNOWLEDGMENTS AND ADDRESSES

Received June 10, 1968, from the *College of Pharmacy, University of Rhode Island, Kingston, RI 02881*

Accepted for publication October 31, 1968.