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## Dielectric Solubility Profiles of Acetanilide and Several Derivatives in Dioxane-Water Mixtures

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The solubilities of acetanilide, *p*-methyl acetanilide, and *p*-ethoxyacetanilide (phenacetin) were determined in dioxane-water mixtures of known dielectric constants. The solubility curves that were obtained showed a multiplicity of peak solubility values as a function of the dielectric constant. These peak solubilities or dielectric requirements for the subject compounds were found to vary to some extent and may reflect solute polarity with respect to acetanilide as the parent compound.

IN A RECENT communication (1), the existence of multiple solubility peaks for the xanthines as a function of the dielectric constants of dioxane-water mixtures was presented. It was felt that this multipeak array might be evidenced for other pharmaceutical solutes as well. To this end, several substances in the antipyretic class were chosen—acetanilide and the *p*-methyl and *p*-ethoxy derivatives of acetanilide. It was felt that these compounds might allow for a qualitative picture in terms of solute polarity and possible dielectric requirement (DR) shifts. These compounds may be representative of substances for which at some future time quantitation of solubility as a function of dielectric constant is needed.

Enhanced solubility of pharmaceutical substances in solvent mixtures may have usefulness in the control of solubility, especially in pharmaceutical vehicles. Enhanced or maximum solubility for various substances has been reported previously as a function of either solvent composition (2-5), dielectric constants (6-8), or

solubility parameters (9, 10). Increased solubility as a function of the dielectric constant of syrup vehicles has also been reported (11). An interesting paper by Gorman and Hall (12), summarizing some aspects of solubility with solubility parameters and dielectric constants, has also been presented.

Thus, the present studies were conducted with a view toward establishing a multiple solubility peak array for drugs in the antipyretic class and to illustrate the possible generalization of multiple solubility peaks for diverse compounds.

### EXPERIMENTAL

**Materials.**—Acetanilide (Eastman-Kodak No. 3 White Label), *p*-methyl acetanilide (Eastman-Kodak No. 425 White Label), phenacetin (Mallinckrodt No. 2244) were the solutes used in this study. Distilled water (pH 6.8-7.2) and *p*-dioxane (Fisher certified D-111) were the solvents used.

**Equipment.**—A Beckman DK-2 was used for the spectrophotometric analysis. An Ainsworth type 12 balance was used for the gravimetric analysis. A Sargent water bath with attendant thermometer unit for equilibration of samples at 25° and temperature control.

**Methods.**—Solvents of dioxane-water mixtures in 2.5% v/v increments were added to 22-ml. screw-capped Teflon-lined vials and excess solute added. Sample vials were tied down to a rotating

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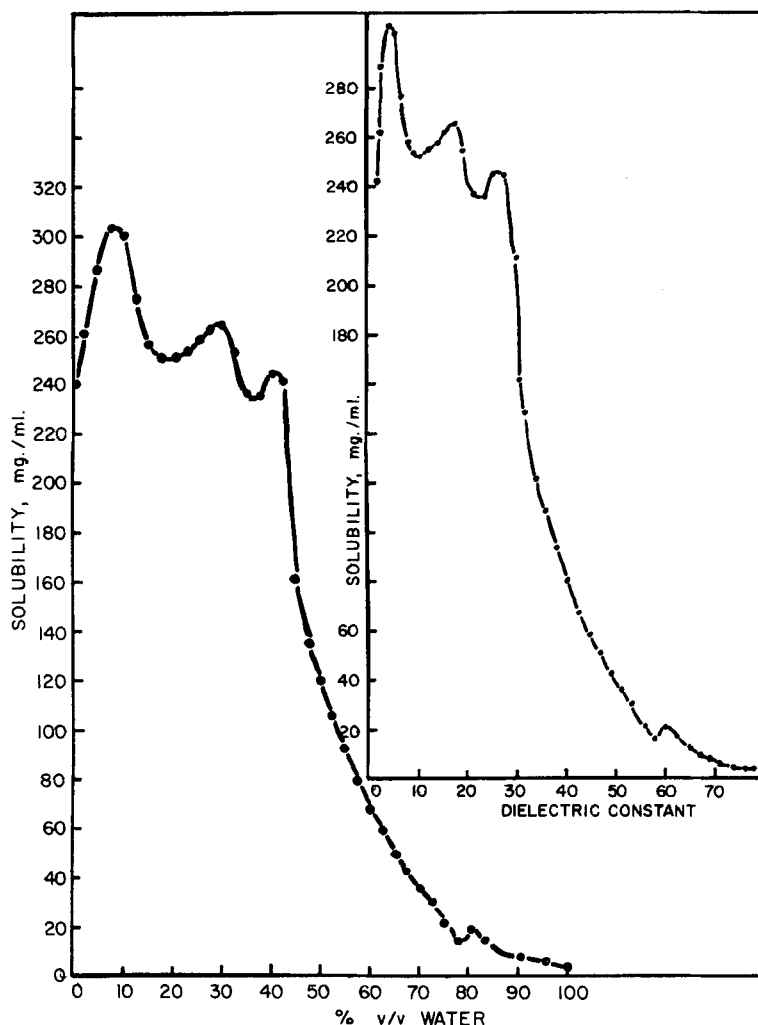


Fig. 1.—The solubility of acetanilide in mg./ml. at 25° as a function of either v/v composition and the dielectric constant (insert) of dioxane-water mixtures.

plastic disk assembly connected to a variable speed motor. A variac was set at a value so that the vial contents were actively agitated. The bath temperature was maintained at  $25 \pm 0.2^\circ$  by means of a Sargent thermonitor unit. An equilibration time of 24 hr. was found to be sufficient in all cases. The solutes were handled directly, and it was felt that no pretreatment was necessary, since they were supplied in crystalline or granular form. The methods of assay and protocol in the solubility determinations have been reported previously (1).

## RESULTS AND DISCUSSION

The solubility dielectric profile of acetanilide is shown in Fig. 1, where the solubility in mg./ml. is plotted *versus* the composition of dioxane-water mixtures. The insert included in this figure represents solubility in mg./ml. as a function of the dielectric constant of the solvent mixtures. The DR's which were observed exist at the following values of the dielectric constant: 5, 18, 28, and 61. Enhanced solubility of acetanilide in dioxane-water mixtures occurs to varying magnitudes, depending upon the composition (or dielectric constant). It should be pointed out that the experimentally

valid peak at  $\epsilon = 61$  is quite small and represents an increase of about 5 mg./ml. and is considered negligible relative to the other peaks wherein increases of 20–80 mg./ml. occur in the peak areas. The solubility of acetanilide has been studied in binary mixtures other than dioxane-water mixtures. Thus, the literature was checked in order to see if the DR's found in dioxane-water mixtures could be found with other systems. The solubility of acetanilide in ethanol-water mixtures has been reported by Seidell (13) and Holleman and Antusch (14). These reported results are plotted in Fig. 2 from the original data. Their results indicate enhanced solubility for acetanilide at 90 and 85% w/w (30°) ethanol and the dielectric constants for these mixtures are about 28–31. The solubility reported by Seidell is at 30°, and the dielectric constant has been corrected to 25° from temperature coefficients and deviations from linearity in previously obtained but unpublished data. These values correlated quite well with the determined value of about 28 in the present study. Gregg-Wilson and Wright (15) have studied the solubility of acetanilide in water and methanol, ethanol, and *n*-propanol mixtures at 20°. These values have been plotted and

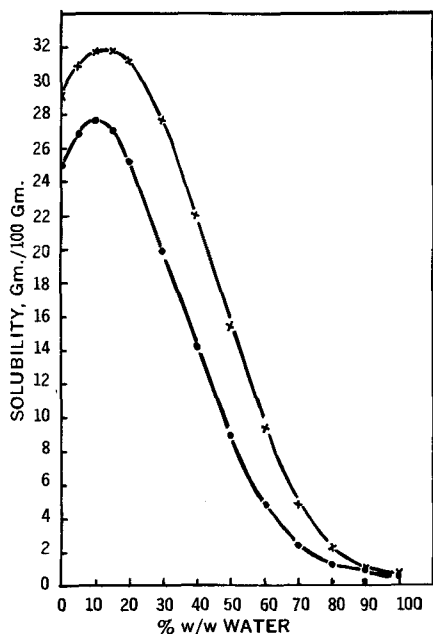


Fig. 2.—The solubilities of acetanilide in Gm./100 Gm. at 25° and 30° in w/w ethanol-water mixtures (13, 14).

are shown in Fig. 3. For the ethanol-water mixtures maximum solubility occurs at about 87% w/w ethanol which has a dielectric constant of 31. However, in the case of water-*n*-propanol mixtures, maximum solubility occurs at a DR of about 23. Mahieu (16) also studied water-propanol mixtures (Fig. 3), and maximum solubility apparently occurs (graphic interpretation) at about 80% w/w

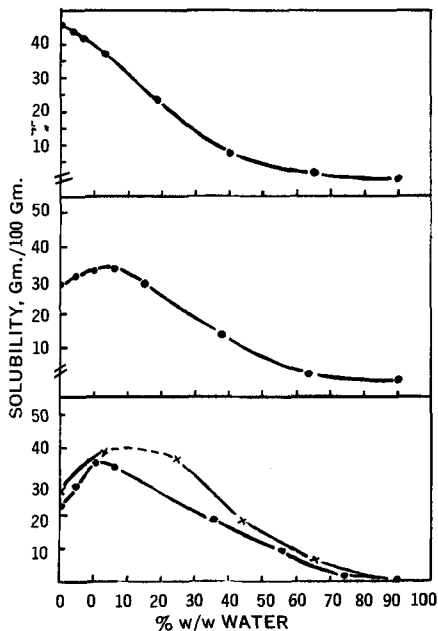


Fig. 3.—The solubility of acetanilide in Gm./100 Gm. of solvent for water-methanol (top), water-ethanol (middle), and water-propanol (bottom) (15, 16).

propanol or a dielectric constant of 26. This latter value is in accord with the present value of 28.

It is interesting to note that a peak solubility does not occur in methanol-water mixtures which may imply that the DR is below or lower than 32, this value being the dielectric constant of pure methanol. The DR values reported above have been corrected to 25° from temperature coefficients (17) and previously obtained data.

For the DR of 18, Gregg-Wilson and Wright (18)

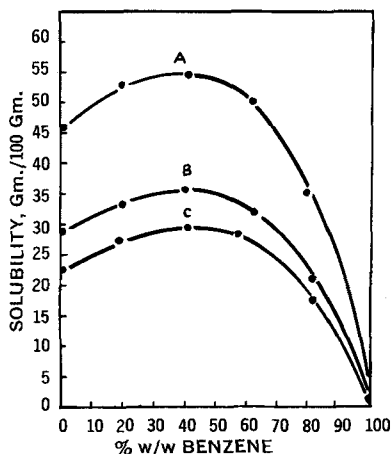


Fig. 4.—The solubility of acetanilide in Gm./100 Gm. of solvent for benzene-methanol mixtures (curve A), benzene-ethanol mixtures (curve B), and benzene-propanol mixtures (curve C) at 20° (18).

report maximum solubility of acetanilide in benzene mixtures with methanol, ethanol, and *n*-propanol. Their results have been plotted and are shown in Fig. 4. From these plots, it seems that the alcohol concentration is about 60% w/w, which gives the following dielectric requirements: benzene-methanol, 19; benzene-ethanol, 16; and benzene-propanol, 12. Both the methanol and ethanol mixtures correlate with the determined value of 18 in the present study. However, the benzene-propanol system is considerably lower in comparison. It is possible that the propyl group causes anomalous behavior in studies of this type.

Other systems bracketing a dielectric constant range of 2 to 32 have also been studied and illustrate some interesting points. Mahieu (16) studied the solubility of acetanilide in nitrobenzene-carbon disulfide mixtures. His results have been plotted in Fig. 5. Unfortunately, it is difficult to pinpoint the solubility maximum. This author has drawn several logical lines (dotted) in this plot attempting to point up the composition of maximum solubility. In this case, if a maximum were assumed to be at 75% w/w nitrobenzene and assuming linearity of dielectric constant with composition the dielectric constant is about 27, this value confirms the present value of 28 in dioxane-water. However, if the maximum solubility is about 60-65% w/w nitrobenzene and assuming linearity, the dielectric constant in this case would be 20-22, which is fair agreement with the determined value of 18.

In another study, Mahieu (16) determined the solubility of acetanilide in nitrobenzene-aniline mixtures with a peak solubility of about 50-60%

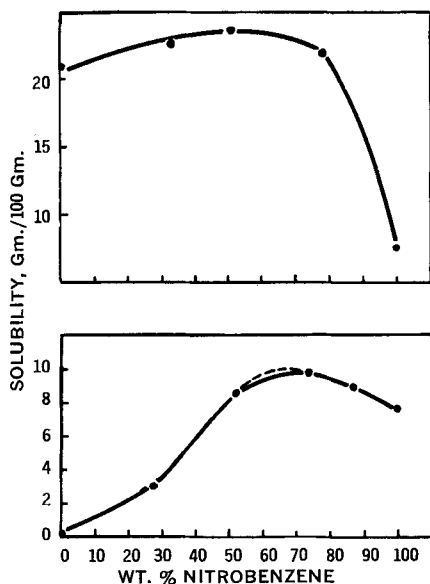


Fig. 5.—The solubility of acetanilide in Gm./100 Gm. of solvent at 25° for nitrobenzene-aniline mixtures (upper) and nitrobenzene-carbon disulfide mixtures (lower) (16).

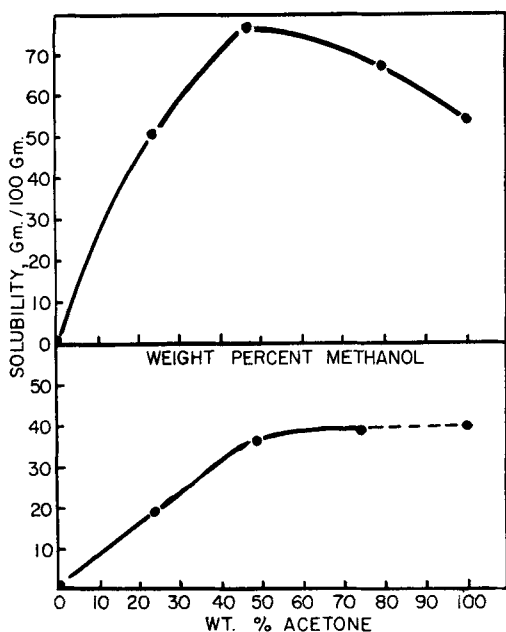


Fig. 6.—The solubility of acetanilide at 25° for methanol-carbon disulfide mixtures (upper) and acetone-carbon disulfide mixtures (lower) (16).

w/w nitrobenzene. At this composition and assuming linearity of dielectric constants for this binary mixture, the DR is 18-20. This again is in fair agreement with the present value. These values are also shown in Fig. 5. Other work by Mahieu shows maximum solubility for acetanilide in methanol-carbon disulfide mixtures and acetone-carbon disulfide mixtures. These results have been plotted and are illustrated in Fig. 6. For the methanol-carbon disulfide mixtures, maximum solubility

occurs at about 46-50% w/w of methanol. Assuming linearity of dielectric constants with composition the DR in these mixtures is about 15-16.

The acetone-carbon disulfide mixture does not show a peak solubility *per se*, but there is a tailing off tendency as one approaches pure acetone. Since the solubility in 75% w/w acetone and pure acetone is very close, the point of 87.5% w/w acetone has been chosen as the midpoint of the asymptotic portion of the curve. This gives a dielectric constant of 17.4, and again linearity of dielectric constant with composition has been assumed. However, one may justifiably choose pure acetone as the limiting value, and the dielectric constant in this case is 20.

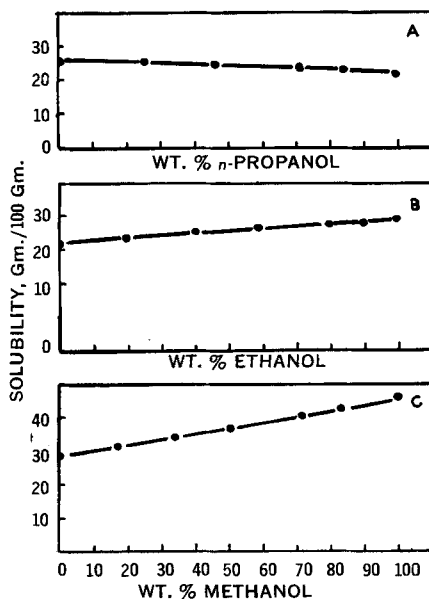


Fig. 7.—The solubility of acetanilide in Gm./100 Gm. of solvent for *n*-propanol-*s*-propanol (A), ethanol-*n*-propanol (B), and methanol-ethanol (C) at 20° (18).

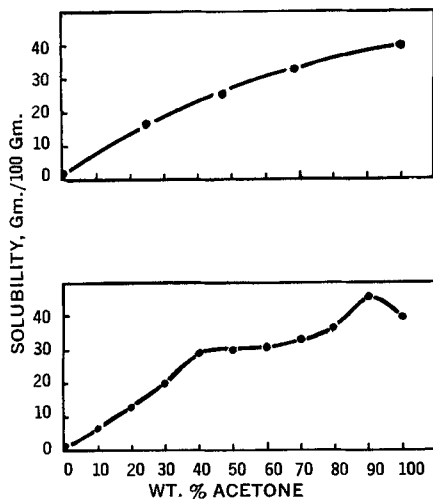


Fig. 8.—The solubility of acetanilide in Gm./100 Gm. of solvent at 25° in acetone-benzene mixtures. Top figure (16); bottom figure (20).

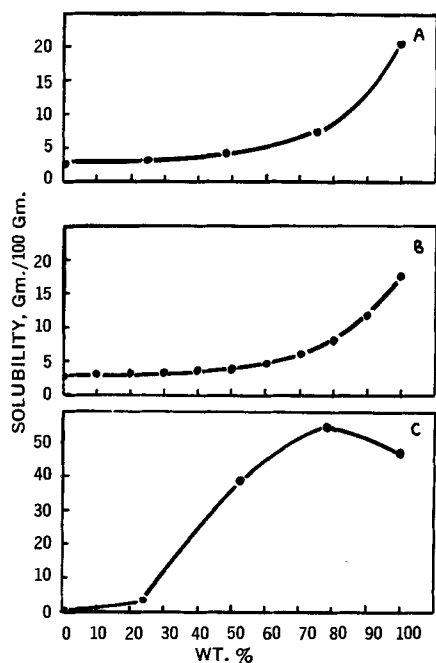


Fig. 9.—The solubility of acetanilide in Gm./100 Gm. of solvent at 25° for ether-chloroform mixtures (curve A and curve B) (16, 20) and for aniline-hexane mixtures (curve C) (16) at 50°.

In both cases as well as the methanol-carbon disulfide system, correlation of these values with the determined value of 18 is quite good. There were several other systems that were studied that merit notice here. Gregg-Wilson and Wright (19) studied the solubility of acetanilide in various alcohol mixtures, these being *s*-propanol-*n*-propanol mixtures, *n*-propanol-ethanol mixtures, and ethanol-methanol mixtures. Their values have been

plotted and shown in Fig. 7. None of these systems shows solubility maxima; however, the first system does show a tailing or constant solubility over a composition range. Since the dielectric constant range for this mixture is about 16-20, any point greater than 50% w/w of secondary propanol should produce a dielectric constant of about 18. This appears to be the case from the plotted data. In the propanol-ethanol system with a dielectric constant range of 20-25, no solubility peak would be expected since the range falls between the maxima of 18 and 28 in this study. However, the ethanol-methanol system with a dielectric constant range of 25-32 should show a solubility maxima at about 50% w/w, but it does not. In fact, the solubility curve is slightly convex down. The nature and polarity of these mixtures may be too close to one another to evidence a maximum.

Studies by Mahieu (16) and Marden and Dover (20) pertaining to the solubility of acetanilide in acetone-benzene mixtures illustrates an interesting point. Their data have been plotted and are shown in Fig. 8. Whereas the data of Marden and Dover show a maximum at  $\epsilon = 18$  and a shoulder at  $\epsilon = 8$ , Mahieu's data show only a slight tailing in solubility going toward pure acetone. The latter data are sparse and may be illustrative of the present concept of small incremental changes in cosolvent composition in order to delineate solubility curves. Mahieu's data are still in keeping with the present DR of 18. Not only does Marden's data show good correlation with the present value, but the shoulder that occurs at a value of about 8 may be identified with the first solubility maximum (DR = 5) found in dioxane-water mixtures.

In the case of the rather surprising solubility maximum at a dielectric constant value of 5, one system has been studied by Mahieu (16)—aniline-hexane mixtures at 50°. Assuming the dielectric constant to vary linearly with composition and taking into account temperature coefficients, the dielectric

TABLE I.—SUMMARY OF THE DR'S FOR ACETANILIDE FROM PRESENT WORK AND PAST LITERATURE

System	DR	Temp., °C.	Ref.	Fig.	Dielectric Constant Range
Dioxane-water <sup>a</sup>	5	25		1	...
Aniline-hexane	5 <sup>b</sup>	50	(16)	9	2-7
Ether-chloroform	...	25	(16, 20)	9	4.3-4.8
Acetone-benzene	8	25	(16, 20)	9	2-20
Dioxane-water <sup>a</sup>	18	25		1	...
Benzene-methanol	19 <sup>b</sup>	20	(18)	4	2-32 <sup>d</sup>
Benzene-ethanol	16	20	(18)	4	2-5
Benzene- <i>n</i> -propanol	12	20	(18)	4	2-20
Acetone-benzene	18	25	(16, 20)	8	2-20
Aniline-nitrobenzene	20	25	(16)	5	6-34 <sup>d</sup>
Methanol-CS <sub>2</sub>	18	25	(16)	6	2-32 <sup>d</sup>
Acetone-CS <sub>2</sub>	17	25	(16)	6	2-20
CS <sub>2</sub> -nitrobenzene	20 <sup>c</sup>	25	(16)	5	2-34 <sup>d</sup>
<i>n</i> -Propanol- <i>s</i> -propanol	18 <sup>b</sup>	20	(18)	7	16-20
<i>n</i> -Propanol-ethanol	...	20	(18)	7	20-25
Ethanol-methanol	...	20	(18)	7	25-32
Dioxane-water <sup>a</sup>	28	25		1	...
Propanol-water	23 <sup>b</sup>	20	(15)	3	20-78
Propanol-water	26	25	(16)	3	20-78
Ethanol-water	32 <sup>b</sup>	20	(15)	3	25-78
Ethanol-water	28 <sup>b</sup>	30	(13)	2	25-78
Ethanol-water	28	25	(14)	2	25-78

<sup>a</sup> DR's from present study. <sup>b</sup> The DR's have been calculated for 25° from temperature coefficients and deviations from linearity from previously obtained data where applicable. In some cases, linearity was assumed and noted under Discussion. <sup>c</sup> Peak or DR may also be at 27. (See Discussion.) <sup>d</sup> These dielectric constant ranges are wide enough to accommodate two peaks; however, only one peak found from given data.

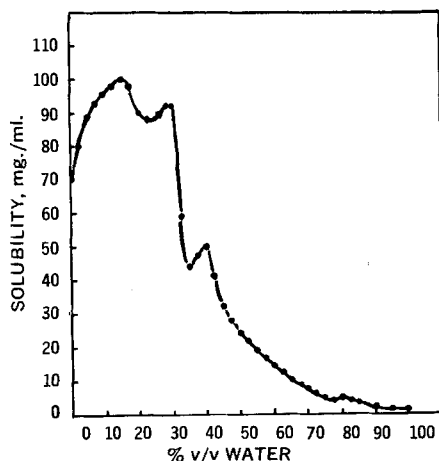


Fig. 10.—The solubility of phenacetin in mg./ml. at 25° as a function of v/v composition of dioxane-water mixtures.

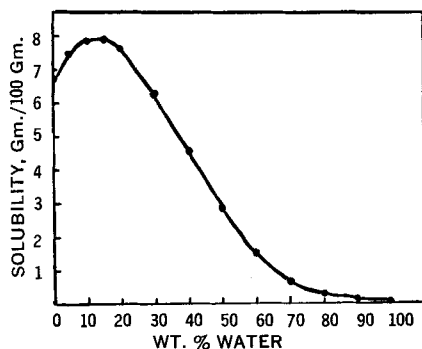


Fig. 11.—The solubility of phenacetin in Gm./100 Gm. of solvent for ethanol-water mixtures at 25° (21).

constant at about 80% w/w aniline and at 25° is about 5. This value agrees with the value obtained in the present study. Mahieu's data have been plotted and shown in Fig. 9. Ether-chloroform mixtures have been studied by both Marden and Dover (20) and Mahieu (16). Their data have been plotted and are also illustrated in Fig. 9. Since the dielectric constant range of these solvent mixtures is 4.3 to 4.8, no solubility maxima should occur. This was found to be the case from the data presented in Fig. 9.

Since the discussion has become rather lengthy, all above data and conclusions attendant to this data have been summarized in Table I. The DR's found in this study are listed, and the systems studied by other workers are given below, each in which the dielectric constant brackets the DR's that were found.

It should be noted that several systems have dielectric constant ranges which could allow for a two solubility peak system, *i.e.*, carbon disulfide-methanol, a dielectric constant range from 2-32. In other words, a peak occurring at DR's of 18 and 28 are possible; however, only one peak at 18 was found from the given data. It may be possible that a swamping effect is operative, *i.e.*, the concentra-

tion is changing at a very rapid rate over small incremental changes of composition. Another possibility is that the published results are sparse and delineation of peaks is difficult.

It is felt that although several approximations have been made, such as assuming linearity of dielectric constants, etc., the correlation of the DR's in past work with the DR's found in the present study is fair to good. The approximate DR's vary over a relatively narrow range of 3-4 dielectric constant units, and this variation has been noted before (6, 8).

Phenacetin, the *p*-ethoxy derivative of acetanilide also showed a four-peak system as a function of the dielectric constant. The solubility of phenacetin in mg./ml. as a function of composition is shown in Fig. 12. Again, it is noted that the experimentally valid peak at 80% v/v water or a dielectric constant of 61 is quite small and is considered insignificant. Although the DR's for phenacetin

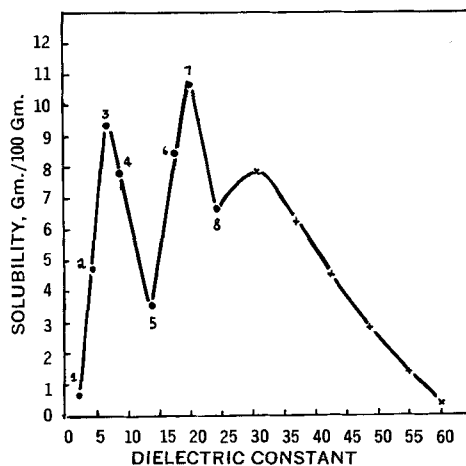


Fig. 12.—The solubility of phenacetin in pure solvents. Key: 1, benzene, 30°; 2, chloroform, 25°; 3, aniline, 30°; 4, quinoline, 25°; 5, amyl alcohol, 25°; 6, benzaldehyde, 30°; 7, acetone, 30°; 8, ethanol, 25°; x, ethanol-water mixtures from Reference 21. All other data also from Reference 21.

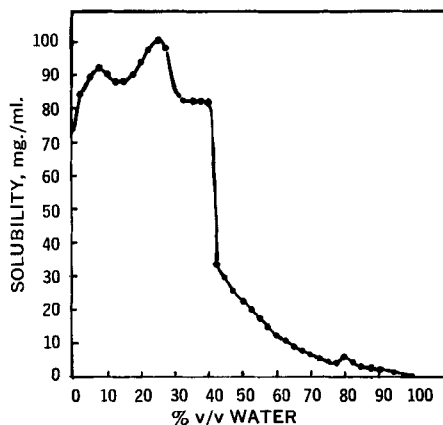


Fig. 13.—The solubility of *p*-methyl acetanilide in mg./ml. at 25° as a function of v/v composition of dioxane-water mixtures.

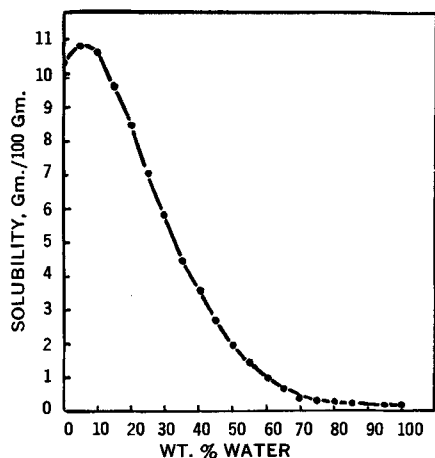


Fig. 14.—The solubility of *p*-methyl acetanilide in Gm./100 Gm. of solvent at 25° in ethanol-water mixtures (23).

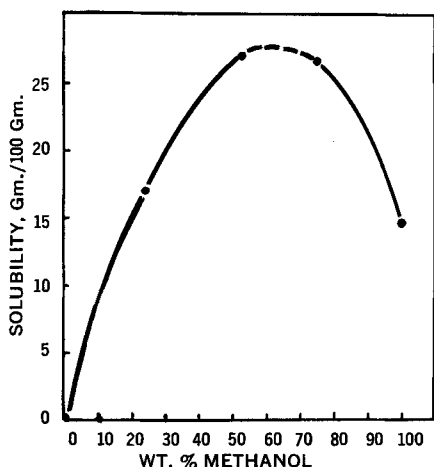


Fig. 15.—The solubility of *p*-methyl acetanilide in Gm./100 Gm. of solvent at 25° in methanol-carbon disulfide mixtures (24).

are similar to those found for acetanilide, it should be noted that the first peak (acetanilide DR 5) has shifted slightly for phenacetin to a value of 8.

Seidell (21) studied the solubility of phenacetin in ethanol-water mixtures (Fig. 11) and found a solubility maxima occurring at about 85% w/w ethanol whose dielectric constant is about 30. This is in fair agreement with the present value of 28. In considering the solubility of phenacetin, enough self-consistent data (21) were available to plot an approximate pure solvent scan. These values have been plotted and are shown in Fig. 12. Obviating temperature differences, it can be seen that solubility peaks are possible at the following values: 7, 20, and 30 which are in fair agreement with the present values. However, this figure is at best a gross approximation. The values for ethanol-water binary mixtures have also been included. One should have far more complete data at a given temperature, but pure solvent scans (8) can be of some use in helping to narrow solubility peak occurrence and their position on the dielectric constant scale.

The solubility of the *p*-methyl derivative of acetanilide was also studied in dioxane-water mixtures, and the results obtained are shown in Fig. 13. Again a four-peak system is observed; the DR's are about the same as the parent compound, except there seem to be small shifts to lower polarity for the second and third DR's relative to acetanilide. This may be due to the polarity of the solute, the methyl group causing not only a shift in the magnitude of solubility, but also a concomitant shift in the polarity. This will be discussed in a latter section of this communication. Other available systems were checked in the literature, and the solubility of *p*-methyl acetanilide in alcohol-water mixtures (22) has been reported. These results have been plotted and are shown in Fig. 14. A peak solubility is observed at 95% w/w ethanol having a dielectric constant of 27, which is in good agreement with the present value of 26 in dioxane-water mixtures. Mahieu (23) studied the solubility of the subject compound in methanol-carbon disulfide mixtures. The results have been plotted and are shown in Fig. 15. Although a solubility maxima trend is obvious, it is difficult, in view of the paucity of data, to delineate the composition of the maxima. However, the midpoint or maxima lies at about 65% w/w methanol, and assuming linearity of dielectric constants, the value at this composition is about 20-22. This binary mixture is wide enough in its dielectric constant range to accommodate two maxima (DR 14 and 26), but only one peak is apparent. Were this system to show a twin peak, the methanol concentrations should be about 45 and 75% w/w, respectively, having dielectric constants of 14 and 26.

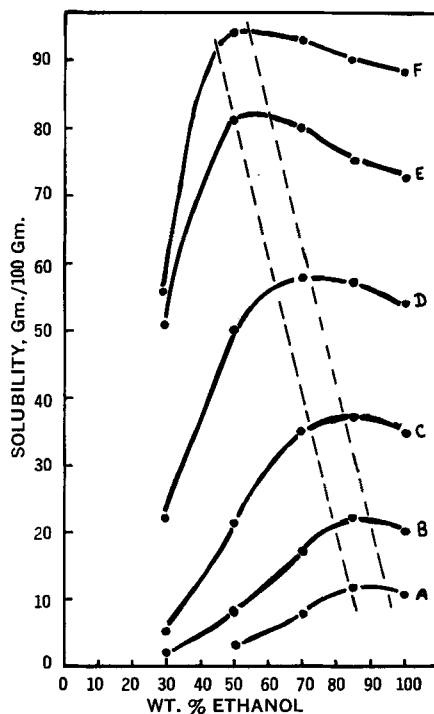


Fig. 16.—The solubility of *p*-methyl acetanilide in Gm./100 Gm. of solvent for ethanol-water mixtures at 30° (curve A), 50° (curve B), 70° (curve C), 90° (curve D), 110° (curve E), 130° (curve F) (25).

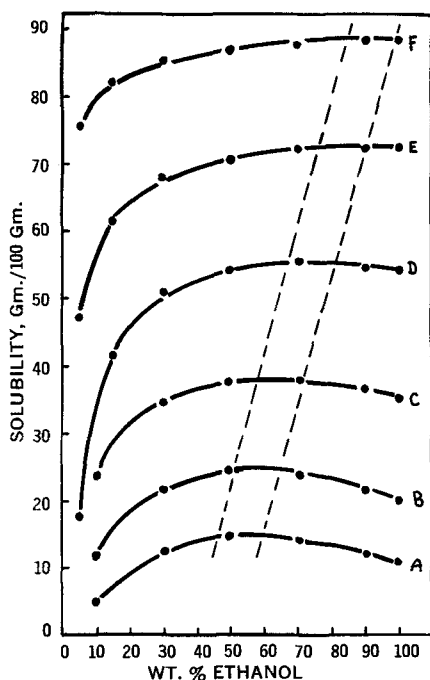


Fig. 17.—The solubility of *p*-methyl acetanilide in Gm./100 Gm. of solvent for ethanol-carbon disulfide mixtures at 30° (curve A), 50° (curve B), 70° (curve C), 90° (curve D), 110° (curve E), 130° (curve F) (25).

Pleuger (24) determined the solubility of *p*-methyl acetanilide in water-ethanol and ethanol-carbon disulfide mixtures at various temperatures. The former mixture fortuitously covers one peak in the dielectric constant span, whereas the latter mixtures cover the DR's for two peaks found in dioxane-water mixtures. Pleuger's data have been plotted and are shown in Figs. 16 and 17. The position of the solubility maxima shifts with increasing temperature as would be expected from decreasing dielectric constants. The expected direction of shift, assuming the DR to be relatively constant, would be toward higher water concentration in ethanol-water mixtures and toward higher ethanol concentration in the ethanol-carbon disulfide mixtures. This trend is obvious from the plotted data. In the case of water-ethanol mixtures a straight line has been drawn from the peak at 30° to the peak at 130°, since these peaks are best defined from the data given. The reason for doing so was that the composition of peak solubility is difficult to pinpoint due to a paucity of data. The composition of the peak solubility at a given temperature was taken from this straight line. Since the peaks may actually reside on one or the other side of this line, the calculations of the DR's as a function of temperature are based on a range of composition around the line drawn. For the water-ethanol mixture, the DR's have been calculated from temperature coefficients (17) and deviations from linearity (3-4 dielectric constant units) from previously obtained data on this system at 25°. It has also been assumed that this deviation is constant or is independent of temperature. Table II illustrates the pertinent data.

TABLE II.—SUMMARY OF THE CALCULATED DR'S FOR *p*-METHYL ACETANILIDE AS A FUNCTION OF TEMPERATURE

Ethanol		Water <sup>b</sup>		Compn. of Peak, % Water	DR	DR <sup>a</sup>
Temp.	$\epsilon$	Temp.	$\epsilon$			
30	23.6	30	76.5	10	29	25-26
50	20.8	50	69.9	10-15	28-29	24-26
70	18.4	70	63.8	17-22	27-28	23-25
90	16.2	90	58.3	27-32	27-26	23-24
100	15.3	100	55.9	...	...	...

<sup>a</sup> DR assuming deviation from linearity to be 3-4 dielectric constant units. <sup>b</sup> Reference 26.

TABLE III.—SUMMARY OF THE CALCULATED DR'S FOR *p*-METHYL ACETANILIDE AS A FUNCTION OF TEMPERATURE

Ethanol		Carbon Disulfide		Ethanol % w/w Peak	DR
$\epsilon$	Temp.	$\epsilon^a$	Temp.		
23.6	30	2.2	30	60	14.2
20.8	50	2.2	50	60-65	12-14
18.4	70	2.2	70	65-70	12-13
16.2	90	2.2	90	75-80	12-13
15.3	100	2.2	100	...	15.3 <sup>b</sup>
14.6	130	2.2	130	~100	14.6

<sup>a</sup>  $d\epsilon/dt$  approximately zero. <sup>b</sup> Dielectric constant of pure ethanol at 100° where solubility becomes asymptotic.

TABLE IV.—SUMMARY OF THE DR'S FOR SUBJECT COMPOUNDS AND THE DIFFERENCE WITH RESPECT TO ACETANILIDE AS THE PARENT COMPOUND

Substance	DR	$\Delta$	DR	$\Delta$	DR	$\Delta$	DR	$\Delta$
Acetanilide	5	...	18	...	28	...	60	...
<i>p</i> -Methyl acetanilide	5	...	14	-4	26	-2	60	...
<i>p</i> -Ethoxy acetanilide	8	+3	18	...	28	...	60	...



In the case of the ethanol-carbon disulfide mixtures, the solubility peaks are slightly clearer; however, the same type of consideration has been applied as for the ethanol-water mixtures. It should be pointed out that these binary mixtures can accommodate two of the maxima found in dioxane-water mixtures, but the first peak or DR 5 was not found. Further, were this maximum to exist in these systems, the ethanol concentration would be about 15%, and it is impossible to tell if it does exist from the published data. In calculating the DR's for the ethanol-carbon disulfide mixtures, it was assumed that the dielectric constants are linear and that no deviations from linearity as a function of temperature occur. Table III illustrates the pertinent data.

The approximate values found in the above analysis correlates rather well the DR found in dioxane-water mixtures. It can therefore be said that there is an indication that the value of the DR for a given substance apparently holds over a wide temperature range.

In these series of compounds, the effect of substituents on a parent compound can be evaluated to an approximate degree. In Table IV, the compounds have been listed with their respective DR's, followed by the difference between the observed peak and acetanilide, which is considered to be the parent compound.

In Table IV, a negative sign indicates a shift to a lower dielectric constant value, whereas a positive sign indicates a shift to a higher dielectric constant value. Unfortunately, the shifts are within the arbitrarily defined limits of three dielectric constant units, so that the  $\Delta$ 's may not have very much meaning in terms of solute polarity. At least there is an indication that the original solute polarity may play a role in the position of the DR on the dielectric constant scale.

In order to support this concept of solute polarity, further studies of the DR's of the *p*-hydroxy derivative are being carried out, and somewhat more striking shifts to higher dielectric constants are being found. Since confirmatory solubility runs are in progress, the DR's cannot be delineated exactly; however, the first DR seems to be about 13-15 (acetanilide DR 5). The other DR's are being checked. In this regard, the solubility of the *p*-sulfamyl derivative in alcohol-water mixtures has been reported (25), and the maximum occurs at about 60% alcohol. Since the concentration notation was

not reported, the DR at 60% v/v or w/w is in the range of 40-43. If it is assumed that the value of this peak should be correlated to the DR of 28 for acetanilide, then the effect of solute polarity is evidenced.

## SUMMARY

Each of the solutes studied essentially showed a three-peak solubility profile which correlated rather well with past work. Multiplex profiles in solvent mixtures spanning two peaks in dioxane-water mixtures were not generally found, which may be due to a swamping effect or a paucity of data.

Solute polarity may play a role in the position of the DR on the dielectric constant scale. There are some indications that this may be true.

Approximate DR correlations are found in given binary mixtures as a function of temperature. The DR's are apparently constant over a relatively wide range of temperature.

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