

Dielectric Constants of Complex Pharmaceutical Solvent Systems II. Water-Ethanol-Sucrose and Water-Ethanol-Sorbitol

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Dielectric constants of water-ethanol-sucrose and water-ethanol-sorbitol systems have been experimentally determined. Dielectric constant values in these systems were generally found to be a complex function of composition expressed as weight per cent. Data are presented which will allow generation of dielectric constant-composition relationships over a dielectric constant range between 40 and 70.

THE PREVIOUS publication in this series (1) presented dielectric constant data for water-ethanol-glycerin and water-ethanol-propylene glycol systems. Dielectric constants were shown to be linear functions of the concentrations of the various components expressed on a per cent by volume basis. Because of various complexities of the systems, however, no simple relationship appeared to exist between dielectric constants of the mixtures and those of the pure components. A simplified form of the Onsager-Kirkwood equation could not be employed to calculate dielectric constants in such systems. It was proposed that precise values for dielectric constants of multicomponent mixtures could best be obtained by experimental measurement. This report presents dielectric constant data for two common pharmaceutical solvent systems, water-ethanol-sucrose and water-ethanol-sorbitol.

EXPERIMENTAL

Materials and Reagents.—The following materials were used without further purification: ethanol, 100% w/w, sucrose U.S.P., and sorbitol, Eastman white-label grade. Distilled water was used to prepare all samples. Reagent grade acetone was used to calibrate the instrument employed in measuring dielectric constants of test samples.

Preparation of Test Samples and Collection of Data.—The procedures for preparing test samples and collecting data were described previously (1). Dielectric constants¹ were determined at 25.0° with a Sargent, model V, chemical oscilloscope standardized with water-acetone mixtures of known dielectric constant (2). Dielectric constant values determined for various test samples in the two solvent systems are shown in Tables I, II, and III.

Treatment of Data.—The composition of all samples in a system which should possess dielectric constant values of 70, 60, 50, etc., was determined from the experimental data by the method described previously (1). Figures 1 and 2 show dielectric constant *versus* composition relationships (isodielectric curves) for the two systems studied. For the reader's convenience in accurately reconstructing these graphs, the data necessary for preparing Figs. 1 and 2 are presented in Tables IV and V. The accuracy of the isodielectric curves shown in Figs. 1 and 2 was checked by measuring the dielectric constants of solutions having compositions picked at random across the total length of each of the various curves. The results are summarized in Table VI.

Received August 11, 1965, from the School of Pharmacy, San Francisco Medical Center, University of California, San Francisco.

Accepted for publication, September 15, 1965.

This investigation was supported by research funds from the Academic Senate, University of California.

¹ The dielectric constant of ethanol used for preparing test samples conformed to accepted values (13).

TABLE I.—DIELECTRIC CONSTANTS OF TEST SAMPLES IN THE WATER-ETHANOL-SUCROSE SYSTEM AT 25.0°C.

Sucrose/ Ethanol	Dielectric Constant Water Content of Test Sample			
	35% w/w	50% w/w	65% w/w	80% w/w
1:0	56.4	64.2	68.0	73.4
4:1	51.2 ^a	60.4	67.0	72.0
	51.8	60.6	66.4	72.6
3:2	48.4	57.1	65.1	71.2
	47.8	56.5	65.5	71.8
2:3	42.7	52.4	62.7	70.0
	42.9	53.6	62.8	70.1
1:4	39.9	48.6	60.4	69.6
	39.8	48.8	60.0	69.6

^a Where two values are listed, they represent dielectric constants of duplicate samples.

TABLE II.—DIELECTRIC CONSTANTS OF TEST SAMPLES IN THE WATER-ETHANOL-SORBITOL SYSTEM AT 25.0°C.

Sorbitol/ Ethanol	Dielectric Constant Water Content of Test Sample				Other
	30% w/w	40% w/w	60% w/w	80% w/w	
1:0	61.4 ^a	...	69.3	72.9	^b
	60.4	...	68.3	72.5	
4:1	54.7	58.8	65.1	71.3	
	54.4	58.3	64.8	70.7	
3:2	47.7	52.7	62.0	69.9	
	48.2	52.9	62.2	70.0	
1:1	46.0	50.4	59.8	69.2	
	45.8	50.8	60.4	69.6	
2:3	43.1	48.6	59.4	69.1	
	42.9	48.2	59.0	69.2	
1:4	39.5	44.5	56.4	68.1	
	38.4	43.9	55.7	67.3	^c
Other ^{d-e}					

^a The two values represent dielectric constants of duplicate samples. ^b 50% w/w—66.8, 65.9; 70% w/w—70.7, 70.5; 90% w/w—74.9, 74.8. ^c 75% w/w—65.5, 65.5; 80% w/w—68.2, 67.8; 85% w/w—70.7, 71.2. ^d 9:1, 77% w/w—70.8, 70.8; 73% w/w—70.0, 70.0; 70% w/w—68.9, 68.8; 36% w/w—61.7, 61.8; 30% w/w—58.8, 58.6; 40% w/w—62.9, 62.5. ^e 1:9, 30% w/w—37.3, 37.2; 35% w/w—39.9, 39.8; 40% w/w—43.0, 43.0. ^f 7:3, 55% w/w—62.2, 62.3; 50% w/w—59.9, 60.3; 45% w/w—57.5, 57.7. ^g 3:7, 35% w/w—43.7, 44.0; 30% w/w—41.1, 41.6; 25% w/w—38.7, 38.9.

DISCUSSION

Results presented in Figs. 1 and 2 are qualitatively similar to those found for other solvent systems (1). The nonlinear relationships between dielectric constant and composition in the system containing sorbitol conform with statements made previously regarding the lack of ability of methods based on calculation to predict accurately the correct dielectric constant values in these systems. The methods

TABLE III.—DIELECTRIC CONSTANTS OF SATURATED SOLUTIONS OF WATER-ETHANOL-SUCROSE AND WATER-ETHANOL-SORBITOL

Ethanol, % w/w	Sucrose, ^a % w/w	Sorbitol, ^b % w/w	Dielectric Constant
92.10	0.40	...	25.1, 25.0
64.10	11.40	...	35.3, 35.3
31.30	39.60	...	43.3, 43.2
15.80	52.90	...	49.1, 49.0
6.00	62.20	...	52.8, 52.7
0	67.60	...	54.8, 54.9
0	...	71.90	60.4, 60.5
2.86	...	68.62	59.3, 59.5
5.74	...	66.02	58.0, 57.3
10.53	...	62.38	54.7, 55.5
14.57	...	57.98	53.4, 53.5
22.37	...	50.45	50.1, 49.8
31.22	...	42.70	45.8, 45.5
42.42	...	33.84	41.2, 41.1
65.72	...	13.64	34.1, 33.8
83.95	...	3.41	28.6, 28.7
91.20	...	1.92	26.2, 26.2

^a Solubility calculated from data of Reber (11). Water content, % w/w = 100% - (% w/w ethanol + % w/w sucrose). ^b Solubility calculated from data of Barr *et al.* (12). Water content, % w/w = 100% - (% w/w ethanol + % w/w sorbitol). ^c Values are for duplicate samples

TABLE IV.—WEIGHT COMPOSITIONS OF THE WATER-ETHANOL-SUCROSE SYSTEM EXPECTED TO GIVE IDENTICAL DIELECTRIC CONSTANT VALUES

Nominal Dielectric Constant Value ^a	Water, % w/w	Ethanol, % w/w	Sucrose, % w/w
70	68.5	0	31.5
	73.5	5.3	21.2
	76.0	9.6	14.4
	81.0	15.2	3.8
	82.8	17.2	0
60	41.0	0	59.0
	49.0	10.2	40.8
	55.5	17.8	26.7
	60.0	24.0	16.0
	65.0	28.0	7.0
50	68.4	31.6	0
	31.2	11.5	57.3
	33.5	13.3	53.2
	38.5	24.6	36.9
	46.0	21.6	32.4
40	52.0	38.4	9.6
	54.3	45.7	0
	28.3	47.5	24.2
	35.0	52.0	13.0
	37.5	62.5	0

^a See Table VI for measured mean dielectric constant value for each curve.

TABLE V.—WEIGHT COMPOSITIONS OF THE WATER-ETHANOL-SORBITOL SYSTEM EXPECTED TO GIVE IDENTICAL DIELECTRIC CONSTANT VALUES

Nominal Dielectric Constant Value ^a	Water, % w/w	Ethanol, % w/w	Sorbitol, % w/w
70	64.6	0	35.4
	73.0	2.7	24.3
	77.0	4.6	18.4
	80.0	8.0	12.0
	81.0	9.5	9.5
	82.4	10.6	7.0
	82.8	17.2	0
	83.2	13.4	3.4
	60	27.5	1.0
32.5		6.8	60.7
43.5		11.3	45.2
50.0		15.0	35.0
56.8		17.3	25.9
59.8		20.1	20.1
62.7		22.4	14.9
66.8		26.6	6.6
68.4		31.6	0
50	34.2	26.3	39.5
	38.6	30.7	30.7
	43.0	34.2	22.8
	49.2	40.6	10.2
	54.3	45.7	0
40	24.7	43.3	32.0
	27.5	50.7	21.8
	33.0	53.6	13.4
	35.7	57.9	6.4
	37.5	62.5	0

^a See Table VI for measured mean dielectric constant value for each curve.

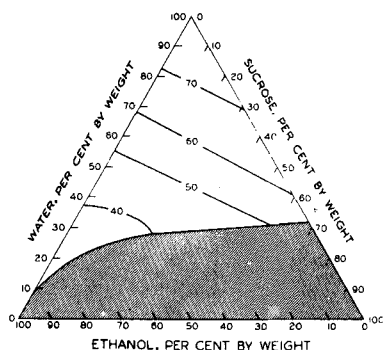


Fig. 1.—Dielectric constant-weight percentage relationships for the system water-ethanol-sucrose. The shaded area represents the region of immiscibility calculated from the data of Reber (11).

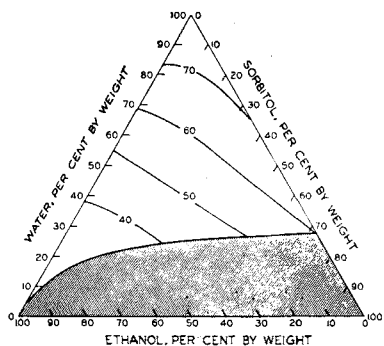


Fig. 2.—Dielectric constant-weight percentage relationships for the system water-ethanol-sorbitol. The shaded area represents the region of immiscibility calculated from the data of Barr *et al.* (12).

usually employed for calculating approximate dielectric constants predict linear relationships between dielectric constant and composition. The linear relationships between composition and dielectric constant seen for the system containing sucrose (Fig. 1) are thought to be fortuitous and do not

TABLE VI.—DIELECTRIC CONSTANT VALUES MEASURED FOR SAMPLES HAVING COMPOSITIONS SPECIFIED BY ISODIELECTRIC CURVES IN FIGS. 1 AND 2

Nominal Dielectric Constant	Measured Mean Dielectric Constant ^a	
	Water-Ethanol-Sucrose	Water-Ethanol-Sorbitol
70	69.2 ± 0.5 ^b	71.1 ± 0.4 ^b
60	59.8 ± 0.3	61.8 ± 0.3
50	50.9 ± 0.3	50.4 ± 0.3
40	40.8 ± 0.7	40.4 ± 0.7

^a Mean value for six samples. ^b 95% confidence interval.

reflect conformity to the linear relationships predicted by theoretical equations based on noninteracting systems. It should also be noted that isodielectric curves in Fig. 1 are not evenly spaced from one another. This shows failure to conform to the predictions of theoretical equations.

Table VI shows that the nominal and the actual dielectric constants for samples chosen from the isodielectric curves in Figs. 1 and 2 differ significantly in some cases. The reasons for such differences have not been determined. It is possible that these deviations originate from interpretations made during the graphical procedures used to generate data for the isodielectric curves. The relatively small magnitude of the confidence intervals about the mean values confirm the validity of the curves with respect to their ability to define isodielectric solutions. Data presented in Tables I, II, and III allow one to determine isodielectric solutions graphically for any desired nominal value of dielectric constant between 40 and 70. Results in Table VI suggest that the actual dielectric constant of such solutions would be within 1 to 3% of the nominal value. Such accuracy is sufficient for most purposes.

Lordi *et al.* (3) have commented that values reported previously (1) for the water-ethanol-glycerin system are not in exact agreement with their results. It was implied that this difference was due to the dielectric constant values assigned to the water-acetone mixtures (2) used in standardizing the oscilometer. It is the authors' opinion that there is no advantage to be gained by using the dielectric constant values assigned to the water-acetone system by Albright (4) as was suggested (3). When one compares the data of Albright with that of Harned and Owen (5), it is found that the values for dielectric constants of water-acetone mixtures used (1) in standardizing the oscilometer are, for the most part, intermediate between these two sets of

data. Since the dielectric constant values used in standardizing the oscilometer are well within the range of values commonly accepted for the water-acetone system, we have not changed our standardization procedure. It might also be pointed out that the water-dioxane mixtures advocated as standards (3) are subject to similar variation (5-7).

The results of this research may be important for uses described previously (1). One such suggested use was for preparing pharmaceutical solvent systems possessing a predetermined degree of polarity. The need for such information originated from the observations of Moore (8) that the solvent dielectric constant may be manipulated to produce dissolution of a solute at a desired concentration and to blend pharmaceutical solvents to a predetermined degree of polarity. This method which relies on the ability of the dielectric constant to serve as an accurate indicator of a solvent's polarity or dissolving power has been questioned (3, 9). Reichardt (10) has discussed various empirical parameters used to describe solvent polarity and has pointed out the inability of the macroscopic dielectric constant to provide a direct measure of interactions on a molecular scale. Thus, while data presented here may be useful to those attempting to follow procedures described by Moore (8), it must be recognized that use of these more accurate dielectric values will not alone insure success of the method. Data presented here and previously (1) will also be useful in various ways to those studying certain physical and chemical processes occurring in these solvent systems.

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