J. Soc. Cosmet. Chem., **34**, 335-350 (November 1983)

Microemulsions: Evolving technology for cosmetic applications

A JAYAKRISHNAN, K. KALAIARASI, and D. O. SHAH,
Departments of Chemical Engineering and Anesthesiology, University of Florida, Gainesville, FL 32611.

Received June 28, 1982. Presented at the Society of Cosmetic Chemists Annual Scientific Meeting, New York, NY, December 10-11, 1981.

Synopsis

The solubilization of hydrocortisone by microemulsions based on the combination of sodium stearate and sodium myristate with various alcohols and hydrocarbon oils was investigated by spectroscopic means at room temperature. The alcohols employed were n-butanol, n-pentanol, n-hexanol, and n-heptanol. The oils ranged from n-hexane (C_6) to n-hexadecane (C_{16}). It was observed that an increase in chain length of alcohols affected the solubility adversely. Changes in surfactant concentration, oil chain length, or water-to-oil ratios in the microemulsions did not have any significant effect on the solubility of the steroid. The solubilization capacity of the microemulsions was comparable to that of pure alcohols.

The formulation of a microemulsion using pharmaceutically acceptable surfactants and hexadecane oil has been achieved. Brij® 35 and Arlacel® 186 were employed as surfactants, while isopropanol was incorporated as the cosurfactant. The microemulsion was stable upto 70°C without undergoing phase separation. Viscosity data suggested that the microemulsion obtained was the water-in-oil type. Electrical conductivity measurements were interpreted in terms of the percolation theory of charge transport. The solubility of hydrocortisone in the system was determined by gravimetric means and was found to be much greater than in isopropanol on a volume basis of alcohol incorporated in the system. As observed in the case of sodium stearate microemulsions, the solubilization capacity was independent of the oil chain length and water-to-oil ratios in these microemulsions. Replacing water by 0.9% NaCl solution did not affect the solubility of hydrocortisone in microemulsions. Possible applications of microemulsions in skin care and cosmetic areas are mentioned.

INTRODUCTION

Drug efficacy can be severely limited by poor solubility in suitable vehicles (1). When small amounts of the drug are to be delivered in accurate dosage forms, thermodynamic stability of the molecules in solutions as opposed to thermodynamic instability in suspensions or dispersions becomes an important criterion. Optimization of solubility is a problem in drug formulations in solutions because drug design does not generally take into account a particular level of solubility. Surfactant solubilization is one of the most widely employed techniques for solubilizing water insoluble drugs. Though considerable attention has been focused in this area in recent years, there has been no major advance in predicting the solubility of drugs in micelles of a given surfactant. There are only a few marketed products which could be considered to be

isotropic solutions of the drug and surfactant (2). A limiting factor in the use of surfactant solubilizers as effective formulation aids is the finite capacity of the micelles for the drug and the stability of the formulation. Surfactant solubilization has advantages. In the micelle, the reactivity of the solute might be different because of the orientation and proximity of the drug molecules. The solute may be protected from attacking species such as hydrogen or hydroxyl ions (3). The ability of the micellar phase to alter the transport properties of the drug is another advantage in surfactant formulations.

Emulsions are widely used in pharmaceutical, cosmetic, and skincare products since they often possess certain advantages not observed when products are formulated in other dosage forms. Emulsification has been widely used in the preparation of dermatological creams and lotions since it facilitates the penetration of the drug into the skin (4). The potency of topical steroids depends on the vehicles used (5). A problem with conventional emulsions is their instability. In general, the droplets in a conventional emulsion have diameters ranging from 0.2 to 50 μm. Microemulsions are much more stable systems with droplet size ranging from 100-1000 Å. Also, they are optically clear; they are formed spontaneously without the aid of high shear equipment. They are stabilized with the combination of an ionic surfactant and a hydrophobic cosurfactant, commonly an alcohol of medium chain length, or with a non-ionic surfactant of optimum HLB (7). Figure 1 schematically illustrates the structure of

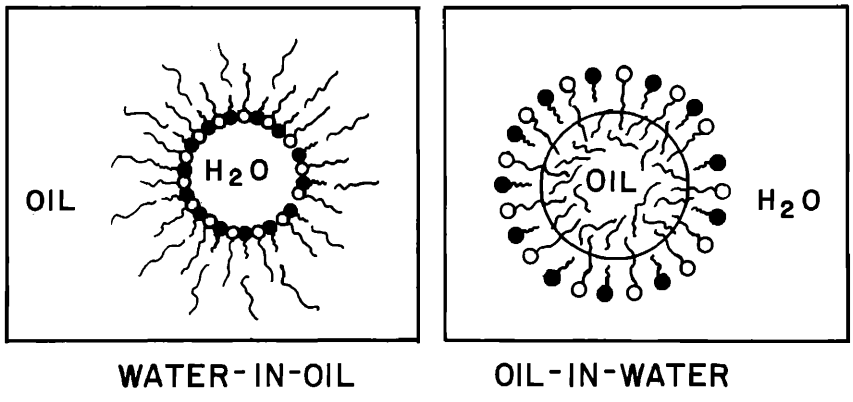

Figure 1. A schematic representation of the structure of water-in-oil and oil-in-water type microemulsions in relation to the orientation of the surfactant and cosurfactant molecules.

water-in-oil and oil-in-water microemulsions and the orientation of the surfactant and cosurfactant molecules at the interface. Ever since their introduction in industry (8) and in the scientific world (9), microemulsions have received considerable attention because of their application in various fields of science and technology (10). The structure and properties of microemulsions were investigated by Schulman *et al.* (11-14), who employed various techniques such as light scattering, x-ray diffraction, electron microscopy, ultracentrifugation, electrical conductivity, and viscometry. The formation and physical properties of microemulsions are influenced by the alkyl chain length of alcohol and hydrocarbons (15-19). Though microemulsion is the most widely used term for describing isotropic, clear, low viscosity dispersions of oil, water, and

emulsifiers, alternate terminology has been proposed by various workers (20–25). A survey of pharmaceutical literature revealed that microemulsions have not been explored at all as vehicles for drug delivery in spite of their unique properties. Thus, the present study was undertaken to explore the potential of microemulsions as drug delivery systems, particularly in the area of topical preparations. The dissolution, solubilization, and stability of hydrocortisone in various vehicles have been reported by previous workers (26–29). In this paper we report some of our findings on the solubilization of hydrocortisone in conventional microemulsions as well as in microemulsions formulated with pharmaceutically acceptable surfactants.

EXPERIMENTAL

The microemulsions were prepared by mixing the surfactant(s), alcohol, hydrocarbon oil, and water in suitable proportions and stirring the mixture to clarity with a magnetic stirrer. Sodium myristate was a K & K laboratories product (Practical grade), and sodium stearate was obtained from ICN Pharmaceutical Company. Both Brij® 35 and Arlacel® 186 were purchased from ICI Americas Inc. Alcohols (Fisher Scientific Company) and oils (Chemical Samples Company or Phillips Petroleum Company) of 99 mol. % purity were used. Micronised hydrocortisone was a gift from Alcon Pharmaceutical Laboratories. Solubility studies in microemulsions based on sodium stearate and sodium myristate as surfactants were carried out by stirring excess of the solid steroid in the solvent at room temperature, centrifuging till clear, and assaying the resulting solution spectrophotometrically at 243 nm. With Brig® 35 and Arlacel® 186 as the surfactants, the spectrophotometric method could not be employed since the surfactants absorbed strongly in the ultraviolet region. Therefore, a gravimetric method was employed. This involved stirring a known excess of the drug in a known volume of the microemulsion and filtering the resulting solution quantitatively through a sintered medium porosity crucible. A known excess of the drug was accurately weighed into a known volume of the microemulsion and was allowed to equilibrate for a period of three hours while the solution was kept stirred magnetically using a teflon coated magnetic bar. After equilibration, the solution was filtered quantitatively through a medium porosity sintered crucible using an aspirator. The drug remaining in the crucible was washed free of the emulsion several times with distilled water and the corresponding oil, and dried at 70°C to constant weight. From the weight of the drug remaining in the crucible, the amount dissolved was computed. The accuracy of the gravimetric method was checked in the case of sodium stearate microemulsions wherein solubility of hydrocortisone could be determined spectrophotometrically. The accuracy of the method was found to be within ±0.5%. Viscosity measurements were carried out in a Cannon-Fenske viscometer at room temperature, while the conductivity data were obtained using a Beckman conductivity bridge.

RESULTS AND DISCUSSION

1. SOLUBILIZATION OF HYDROCORTISONE IN MICROEMULSIONS BASED ON SODIUM STEARATE AND SODIUM MYRISTATE AS SURFACTANTS

The maximum solubilities of hydrocortisone in various pure alcohols are given in Figure 2. The solubility of hydrocortisone in water has been reported to be 7.43×10^{-3}

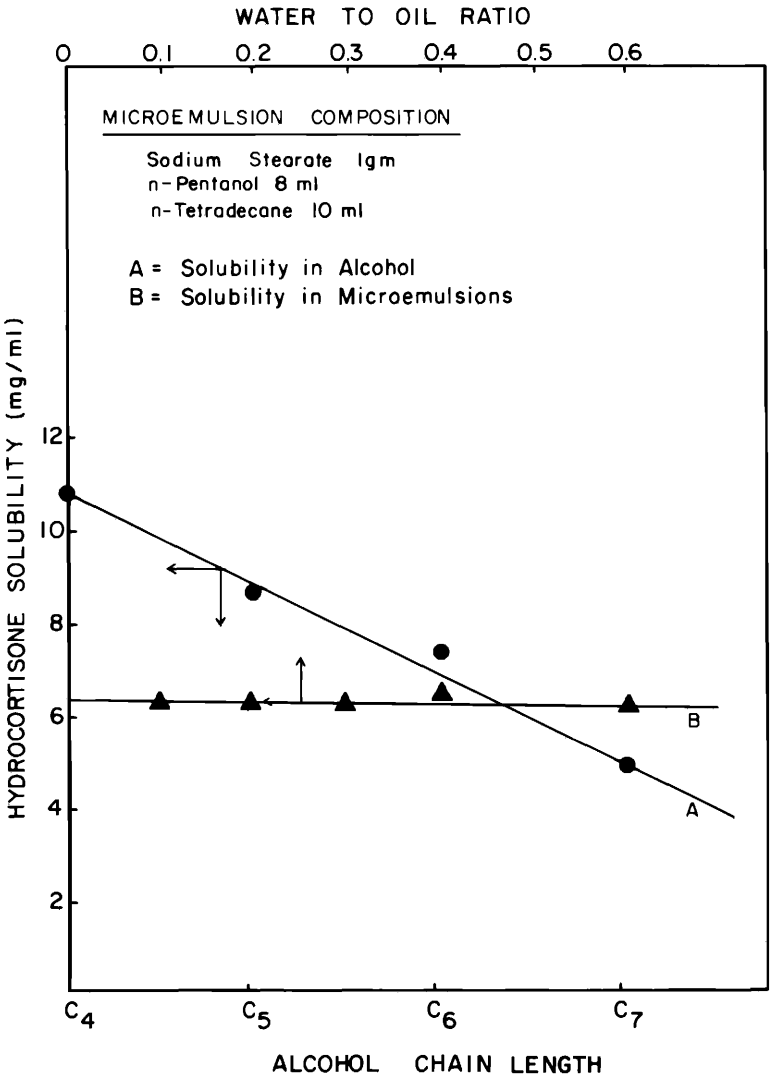

Figure 2. The solubility of hydrocortisone in alcohols of various chain lengths (A), and in microemulsions as a function of water-to-oil ratio (B).

mol. dm^{-3} at 20°C (27). It is practically insoluble in hydrocarbon oils. The solubility of hydrocortisone in microemulsions based on sodium stearate, various alcohols and oils at a water-to-oil ratio of 0.10 are given in Table I. It can be seen that the solubility is maximum with n-butanol and minimum with n-heptanol (Figure 2, Line A). Considering the volume fraction of alcohols present in these systems, it may be noted that the solubility of the steroid in unit volume of the microemulsion is at least twice greater than that in pure alcohols. Though an increase in oil chain length results in an increase in the solubility of the drug, the effect is much less marked than when the chain length of alcohols is varied. An increase in water-to-oil ratios is without any effect on the solubilization capacity of these microemulsions (Figure 2, Line B). Also, changes in

Table I
Dependence of Solubility of Hydrocortisone on Alcohol and Oil Chain Length in Sodium Stearate Microemulsions at 20°C

System	Max. Solubility of Hydrocortisone mg/ml
Sodium Stearate/butanol/hexane	7.32
Sodium Stearate/butanol/decane	7.70
Sodium Stearate/butanol/tetradecane	8.70
Sodium Stearate/pentanol/hexane	5.05
Sodium Stearate/pentanol/decane	6.06
Sodium Stearate/pentanol/tetradecane	6.30
Sodium Stearate/hexanol/hexane	4.30
Sodium Stearate/hexanol/decane	4.92
Sodium Stearate/hexanol/tetradecane	5.05
Sodium Stearate/heptanol/hexane	3.53
Sodium Stearate/heptanol/decane	3.78
Sodium Stearate/heptanol/tetradecane	3.65

All systems with 1 gram sodium stearate, 8 ml alcohol, 10 ml oil, and 1 ml water.

surfactant concentration bring about only slight changes in the maximum solubilization capacity of the steroid (Table II).

With sodium myristate as the surfactant, similar trends were observed. The sodium myristate microemulsions unlike those based on sodium stearate were turbid when prepared due to insoluble impurities present in the surfactant, but became clear when spun in a centrifuge at 5000 rpm for 15-20 minutes. Such clear emulsions were employed for solubility studies. Representative data are tabulated (Table III).

Thus, it is evident that the drug solubilization capacity of microemulsions is better than that of pure alcohols on a volume basis of alcohol incorporated in the system. It should be emphasized that other components of microemulsions do not solubilize hydrocortisone to any significant extent. It has been reported that the presence of non-ionic surfactants facilitates the dissolution and solubility of water insoluble drugs by incorporation in micelles (27-28). It is felt that in these microemulsions, the drug

Table II
The Effect of Sodium Stearate Concentration On Solubility of Hydrocortisone in Microemulsions at 20°C

System	Max. Solubility of Hydrocortisone. mg/ml
Sodium Stearate/butanol/tetradecane	8.7*
	9.34**
Sodium Stearate/pentanol/tetradecane	6.30*
	7.58**
Sodium Stearate/hexanol/tetradecane	5.05*
	5.68**
Sodium Stearate/heptanol/tetradecane	3.66*
	4.67**

*With 1 gram sodium stearate, 8 ml alcohol, 10 ml oil, and 2 ml water.
**With 2 gram sodium stearate, 8 ml alcohol, 10 ml oil, and 2 ml water.

Table III
The Effect of Alcohol Chain Length On Solubility of Hydrocortisone in Sodium Myristate Microemulsions at 20°C

System	Max. Solubility in mg/ml
Sodium Myristate/butanol/decane	8.21
Sodium Myristate/butanol/tetradecane	8.83
Sodium Myristate/pentanol/decane	6.56
Sodium Myristate/pentanol/tetradecane	5.80
Sodium Myristate/hexanol/decane	5.30
Sodium Myristate/hexanol/tetradecane	4.97
Sodium Myristate/heptanol/decane	3.80
Sodium Myristate/heptanol/tetradecane	3.66

All systems with 1 gram sodium myristate, 8 ml alcohol, 10 ml oil, and 1 ml water.

molecules are predominantly situated at the oil-water interphase with their hydrophilic groups directed towards the water pool. The slight increase in solubility with increase in oil chain length for butanol, pentanol, and hexanol containing microemulsions could perhaps be attributed to the increase in the alcohol/soap molar ratio at the interface as reported by Bansal *et al.* (30).

2. PREPARATION AND CHARACTERIZATION OF PHARMACEUTICAL MICROEMULSIONS

Brij® 35 and Arlacel® 186 were employed as surfactants, and isopropanol was incorporated as the cosurfactant in the formulation. The formulation was achieved by mixing the surfactants in suitable proportions, adding oil and isopropanol, and titrating the system against water to clarity with magnetic stirring. We found that the HLB approach was not of much use in the formulation of these microemulsions although it has been reported to be useful in the formulation of macroemulsions. The formulation of a microemulsion was thus an empirical job. Table IV shows the maximum amount

Table IV
Maximum Solubilization of Water in Pharmaceutical Microemulsions with Various Concentrations of Surfactants

Arlacel® 186 in gms	Brij® 35 in gms	Maximum Water Solubilized in ml
1	5	0
1	4	0
1	3	0
1	2	0
2	4	3.1
2	3	2.0
2	2	1.3
2	1	0.5
3	3	2.5
3	2	2.6
3	1	2.1
4	2	7.0
4	1	4.0
5	1	8.2
6	0	1.4

All systems contain 10 ml n-decane oil and 4 ml isopropanol.

of water that can be solubilized in microemulsions with 10 ml of n-decane oil and 4 ml of isopropanol and various amounts of surfactants as indicated . It is seen that with an increase in the concentration of the oil soluble surfactant Arlacel® 186, the water solubilization capacity of the microemulsion is increased (Figure 3). Of course, the

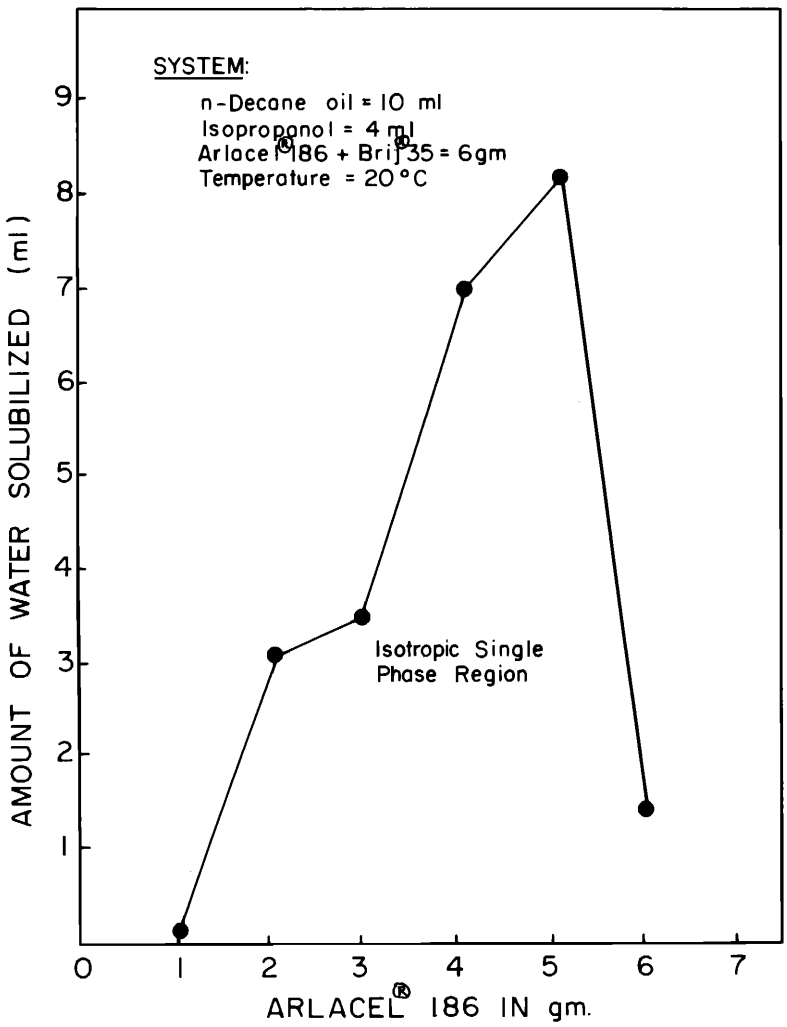

Figure 3. The effect of Arlacel® 186/Brij® 35 ratio on the solubilization of water in microemulsions.

water solubilization capacity of the microemulsions depends on the amount of alcohol as well as the chain length of oil employed. This is illustrated in Figure 4. With 3 ml of isopropanol and 10 ml of oil, the water solubilization capacity of the microemulsions increased from 5.0 ml to 5.9 ml when the oil chain length was increased from C_8 to C_{16}. An increase in concentration of isopropanol at fixed concentrations of the surfactant and oil results in an increase in water solubilization followed by a decrease (Figure 5). The decrease in the water solubilization capacity at higher isopropanol concentrations

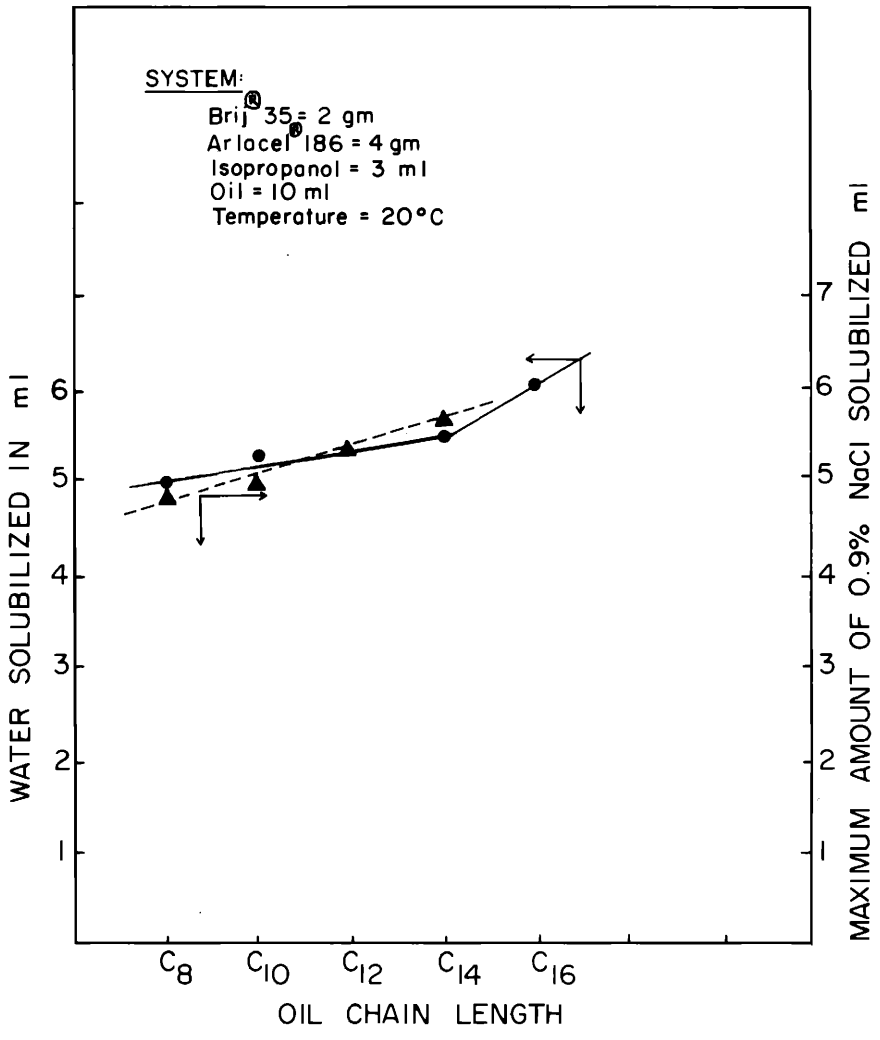

Figure 4. The effect of oil chain length on solubilization capacity of water and saline in microemulsions.

might be due to increased solubilization of the surfactant at the interface in the alcohol and its partitioning into the oil phase since isopropanol is miscible with the hydrocarbon oils.

Replacing water by 0.9% NaCl solution showed interesting results. With 10 ml of various oils and 3 ml of isopropanol, microemulsions with the same amount of surfactant solubilized various amounts of saline (Figure 4). With octane and decane oils, the maximum brine solubilization was followed by the appearance of turbidity and phase separation similar to that in the presence of water. However, with dodecane and tetradecane, the initial isotropic region was followed by a viscous and birefringent region which was not observed with water. With hexadecane oil, the behavior was totally different from the rest of the oils so that even after the addition of 9 ml of 0.9% NaCl solution, though the system became more viscous and slightly hazy, no

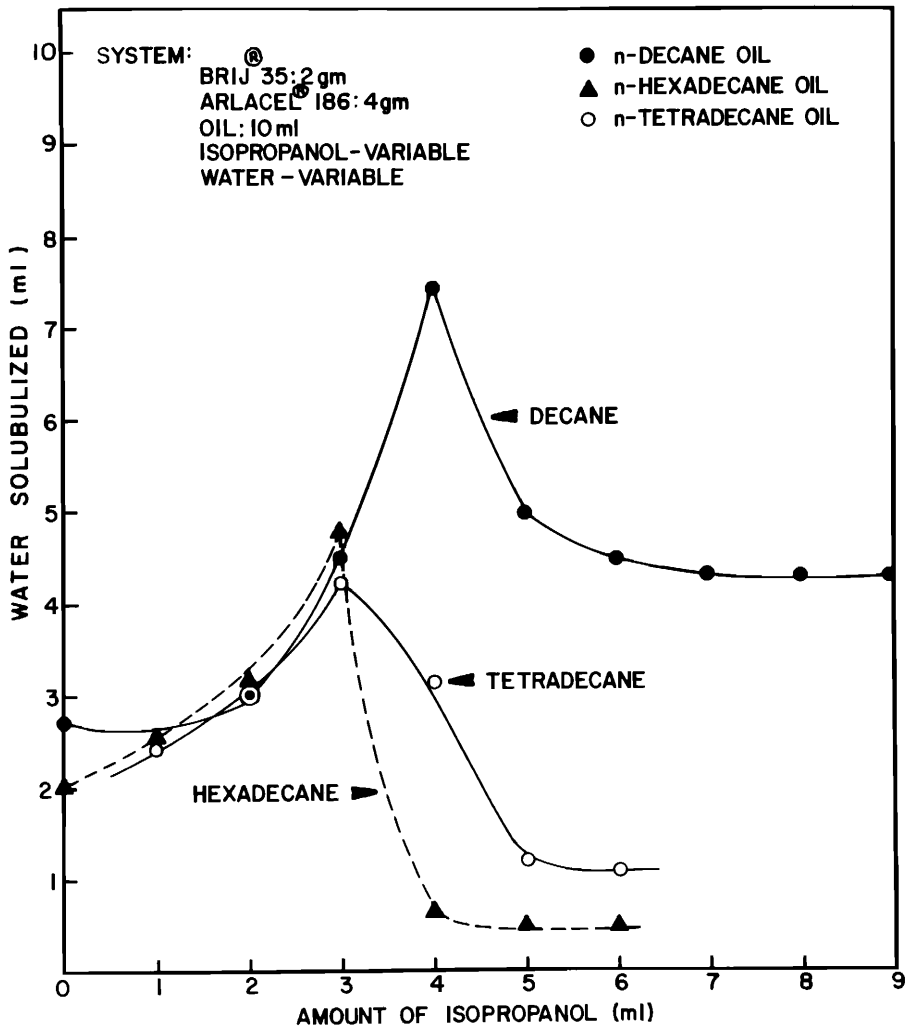

Figure 5. Maximum solubilization of water at various isopropanol concentrations in microemulsions with different oils.

birefringence could be observed. We are not able to offer any logical explanation for this phenomenon at this juncture.

Measurements of the viscosity of the microemulsions indicated that with an increase in water-to-oil ratio, the kinematic viscosity increased steadily suggesting that the microemulsion is the water-in-oil type. This observation is in accordance with the known behavior of dispersions where the viscosity increases with increasing volume of the discontinuous phase (31-32). Representative data with tetradecane as oil at various water-to-oil ratios are plotted in Figure 6. Electrical conductance of the pharmaceutical microemulsion with various oils increased with an increase in water-to-oil ratio. Data obtained with pentadecane oil is given Figure 7. The electrical conductivity was found to increase steeply over five orders of magnitude when the concentration of the droplets was increased. The sharp increase in conductance with an increase in the

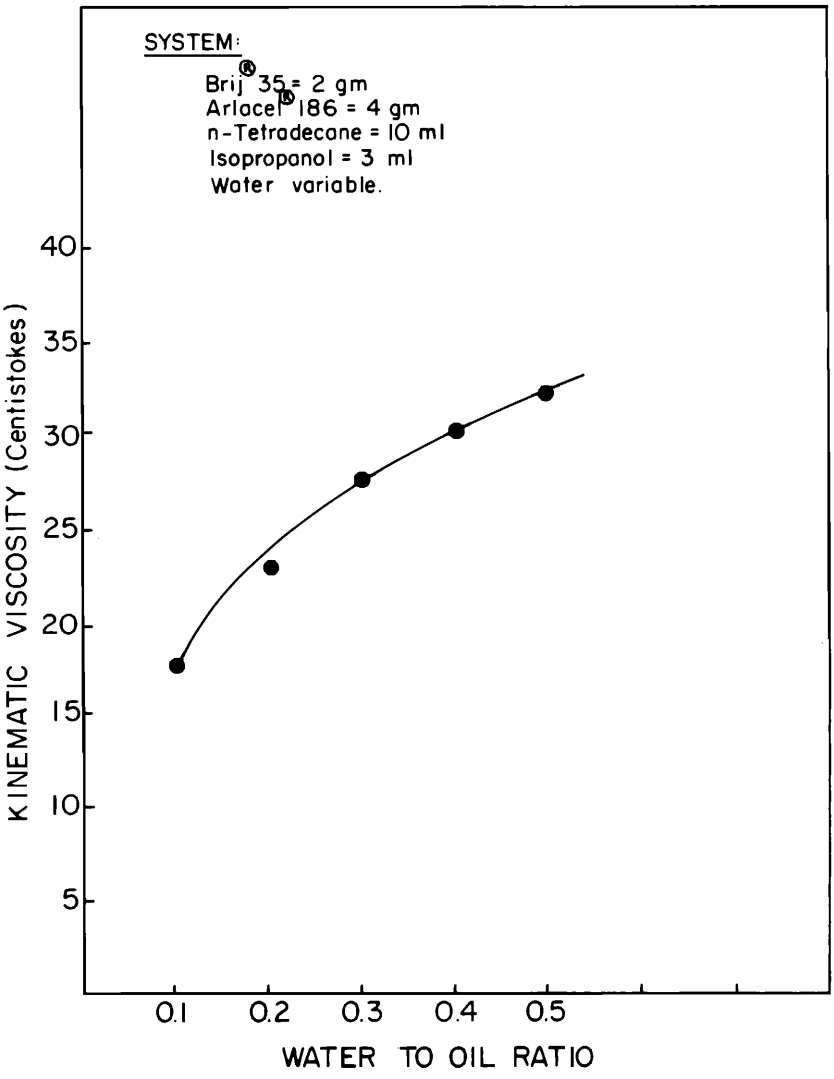

Figure 6. The effect of water-to-oil ratio on the kinematic viscosity of microemulsions.

water-to-oil ratio could be attributed to a percolation transition which gives rise to a continuous path through aggregated droplets beyond a critical volume concentration of droplets (33-34).

3. SOLUBILITY OF HYDROCORTISONE IN PHARMACEUTICAL MICROEMULSIONS

Solubility of hydrocortisone in isopropanol was determined spectrophotometrically. The maximum solubility obtained by this method (8.5 mg/ml) agreed with the value obtained gravimetrically (8.55 mg/ml). It was observed that the solubility of hydrocortisone was greater in isopropanol/water mixtures than in pure isopropanol. The solubility exhibited a maximum when 20% water was present in the alcohol and then

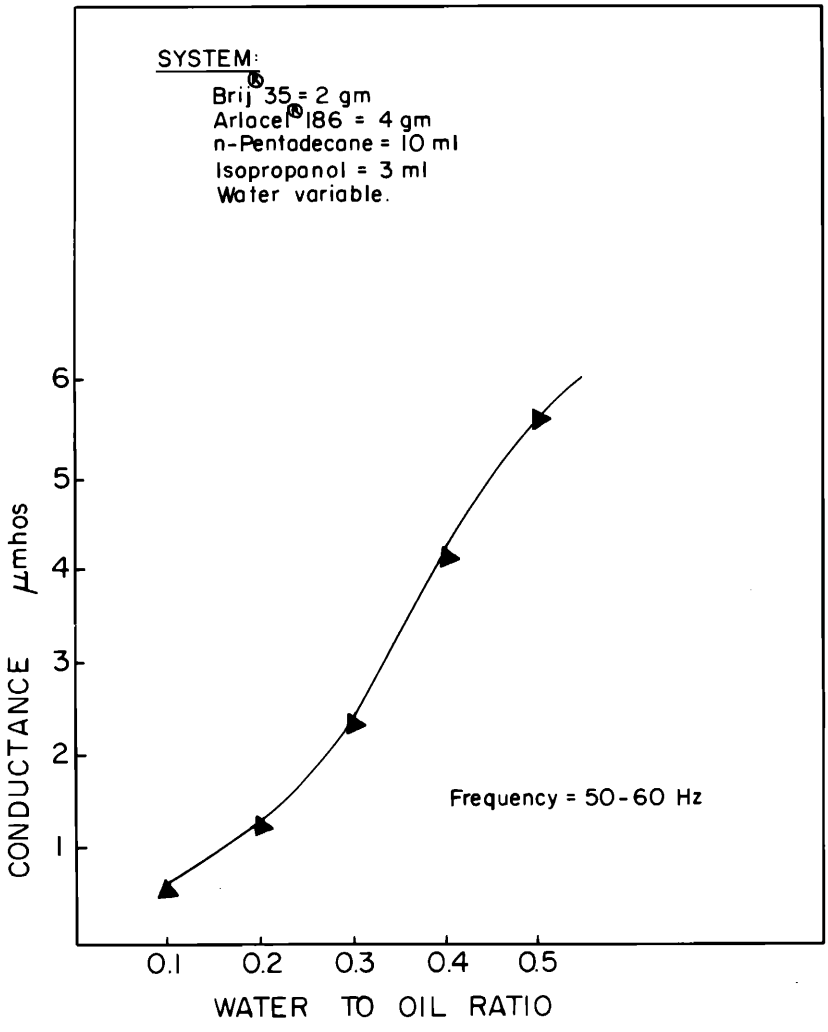

Figure 7. The effect of water-to-oil ratio on the conductance of microemulsions.

dropped off with further addition of water (Figure 8). The maximum solubility is a result of the polarity of the medium reaching the polarity of the drug (33). The influence of polarity of the medium was further confirmed by the determination of solubility in isopropanol-tetradecane mixtures and glycerol-isopropanol mixtures (Figures 8 and 9).

The solubility of the steroid in microemulsions was determined by gravimetric means, since spectrophotometry could not be employed due to strong absorption of the surfactants in the ultraviolet region. As in the model system, the maximum solubility was independent of the water-to-oil ratio within the limits of experimental error (Table V). Also, the solubility was found to be independent of the oil chain length (Table VI). Replacing water by 0.9% NaCl did not change the steroid solubility (Table VI). Thus, as in the model system, the solubility of the steroid in these microemulsions is greater than that in the alcohol on a volume basis of alcohol present per unit volume of the

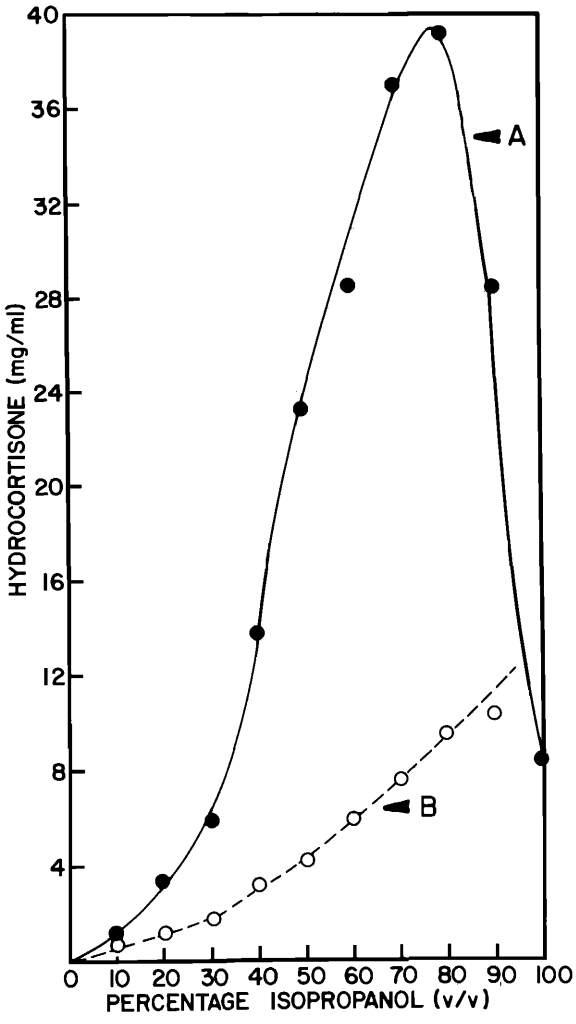

Figure 8. Solubility of hydrocortisone in isopropanol-water mixtures (A), and isopropanol-tetradecane mixtures (B).

microemulsion. Since the drug solubility as before was found to be independent of the water-to-oil ratio as well as the chain length of the oil employed, the mechanism of solubilization could be the same as in the model system. All microemulsions were found to be stable up to a temperature of 70°C. Spinning the microemulsions in a centrifuge at 5000 rpm for two hours did not induce phase separation. Incorporation of 2 ml of carnation mineral oil along the hexadecane oil was found to yield a microemulsion which did not undergo phase separation when kept at 40°C for more than two months, though the mineral oil alone failed to give any microemulsion.

Thus, it appears that when judiciously formulated, microemulsions are potential vehicles for topical applications. In contrast to macroemulsions, they are clear, isotropic, and stable. Because of the small particle size, the total interfacial area is much greater in microemulsions than in macroemulsions. Thus, besides the several known

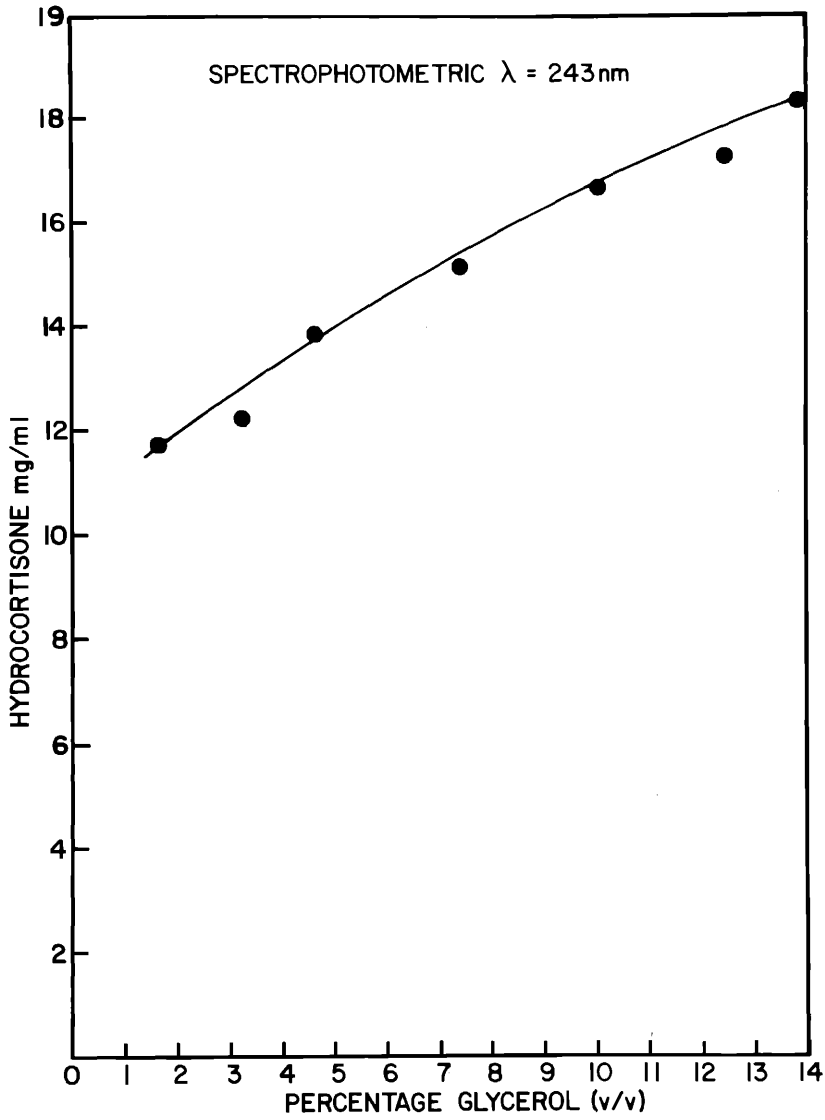

Figure 9. Solubility of hydrocortisone in isopropanol-glycerol mixtures of various compositions.

Table V
Maximum Solubility of Hydrocortisone in n-Decane Microemulsions at Various Water-to-Oil Ratios

Water-to-Oil Ratio	Max. Solubility in mg/ml
0.1	8.30
0.2	8.51
0.3	6.85
0.4	7.35
0.5	7.10

System: n-Decane = 10 ml
Isopropanol = 4 ml
Arlacel® 186 = 4 gm
Brij® 35 = 2 gm
Temperature = 20°C

Table VI
Maximum Solubility of Hydrocortisone in Microemulsions with Various Oils

Oil	Max. Solubility in mg/ml
n-Octane	8.2
n-Tetradecane	8.5, 8.3*
n-Pentadecane	7.8
n-Hexadecane	8.1

System: oil = 10 ml, Isopropanol = 3.5 ml, Arlacel® 186 = 4 gm, Brij® 35 = 2 gm, Water = 3 ml, Temperature = 20°C.
*With 3 ml of 0.9% NaCl.

uses and applications of microemulsions (36–43), they can also serve as vehicles for oil soluble, water soluble, and interphase soluble species for cosmetic and pharmaceutical formulations.

Formulations of microemulsions with low concentrations of the surfactants and pharmaceutically acceptable alcohols and oils are under way. The kinetics and mechanism of dissolution, solubilization, as well as the stability of certain cortisteroids in such microemulsions, will be reported elsewhere.

CONCLUSIONS

1. The solubility of hydrocortisone was found to decrease with an increase in chain length of alcohols, the solubility being the maximum in n-butanol and minimum in n-heptanol.
2. In conventional microemulsions, the solubility of hydrocortisone was found to be independent of the water-to-oil ratio. An increase in oil chain length did not have any significant effect on the solubility of the steroid.
3. The solubility of hydrocortisone was adversely affected by increasing the chain length of alcohol in the microemulsion system, as in the case of pure alcohols. The solubility was comparable to that in pure alcohols.
4. The water solubilization capacity of pharmaceutical microemulsions increased with an increase in concentration of the oil soluble surfactant Arlacel® 186. The water solubilization was maximum at 5:1 (wt/wt) ratio of surfactants Arlacel® 186 and Brij® 35. Either Brij® 35 or Arlacel® 186 alone in combination with oil and isopropanol was not very effective in solubilizing water.
5. Replacing water with 0.9% NaCl in the system gave rise to viscous birefringent systems with dodecane and tetradecane as oils. With octane and decane as oils this behavior was not observed, and the transition was similar to that observed with water.
6. Viscosity data indicated that the pharmaceutical microemulsions were of the water-in-oil type.
7. Solubility of hydrocortisone in pharmaceutical microemulsions was comparable to that in isopropanol. On a volume basis of alcohol incorporated per unit volume of the microemulsion, the solubility of hydrocortisone was found to be six fold higher

in a microemulsion containing 6 gm of the total surfactant, 10 ml of oil, and 3.5 ml of alcohol at a water-to-oil ratio of 0.10 as compared to that in pure isopropanol.

ACKNOWLEDGMENT

The authors wish to express their thanks to Owen-Alcon Laboratories, Fort Worth, Texas for their unrestricted research grant, and the support provided by the University of Florida to carry out this research.

REFERENCES

(1) S. H. Yalkowsky, in Techniques of solubilization of drugs, *Drugs and the Pharmaceutical Sciences,* **Vol. 12,** ed. S. H. Yalkowsky (Marcel Dekker, Inc., 1981), p vii.
(2) A. T. Florence, in Techniques of solubilization of drugs, *Drugs and the Pharmaceutical Sciences,* **Vol. 12,** ed. S. H. Yalkowsky (Marcel Dekker, Inc., 1981), Chapter. 2.
(3) J. M. Brown, *Colloid Science,* **Vol. 3** (Chemical Society, London, 1979).
(4) *Remington Pharmaceutical Sciences,* 15th Ed. (Mack Publishing Co., Easton, 1973), p 327.
(5) Facts and comparisons, *Drug Information* (1980), ed. Edwin K. Kastrup, p 1607.
(6) V. K. Bansal, K. Chinnaswamy, C. Ramachandran, and D. O. Shah, Structural aspects of microemulsions using dielectric relaxation and spin label techniques, *J. Colloid Interface Sci.,* **72,** 524-537 (1979).
(7) S. Friberg, in *Microemulsions: Theory and Practice,* ed. L. M. Prince (Academic Press, New York, 1977), p 133.
(8) V. R. Kokatnur, U.S. Patent, 2,111,100 (1935).
(9) T. P. Hoar and J. H. Schulman, Transparent water-in-oil dispersions: The oleopathic hydro-micelle, *Nature,* **152,** 102-103 (1943).
(10) L. M. Prince, ed., *Microemulsions: Theory and Practice* (Academic Press, New York, 1977).
(11) J. H. Schulman and D. P. Riley, X-ray investigation of the structure of transparent oil-water disperse systems I., *J. Colloid Sci.,* **3,** 383-405 (1948).
(12) J. H. Schulman and J. A. Friend, Light scattering investigation of the structure of oil-water disperse systems II, *J. Colloid Sci.,* **4,** 497-509 (1949).
(13) J. H. Schulman, W. Stoeckenius, and L. M. Prince, Mechanism of formation and structure of microemulsions by electron microscopy, *J. Phys. Chem.,* **63,** 1677-1680 (1959).
(14) W. Stoeckenius, J. H. Schulman, and L. M. Prince, The structure of myelin figures and microemulsions as observed with the electron microscope, *Kolloid Z.,* **169,** 170-180 (1960).
(15) C. E. Cooke and J. H. Schulman, in *Surface Chemistry,* ed. P. Ekwall, K. Groth, and V. Runn Strom-Ries (Academic Press, New York, 1965) pp 231-251.
(16) W. I. Higuchi and J. Misra, Solubilization in nonpolar solvents: Influence of the chain length of solvent on the solubilization of water by dioctyl sodium sulfosuccinate, *J. Pharm. Sci.,* **51,** 455-458 (1962).
(17) S. G. Frank and G. Zografi, Solubilization of water by dialkyl sodium sulfosuccinates in hydrocarbon solutions, *J. Colloid Interface Sci.,* **29,** 27-35 (1969).
(18) D. O. Shah, R. D. Walker, Jr., W. C. Hsieh, N. J. Shah, S. Dwivedi, J. Nelander, R. Pepinsky, and D. W. Deamer, SPE Paper 5815 Presented at Improved Oil Recovery Symposium of SPE of AIME, Tulsa, Oklahoma, March 22-24, 1976.
(19) E. Sjoblom and S. Friberg, Light scattering and electron microscopy determinations of association structures in W/O microemulsions, *J. Colloid Interface Sci.,* **67,** 16-30 (1978).
(20) W. Gerbacia and H. L. Rosano, Microemulsions: Formation and stabilization, *J. Colloid Interface Sci.,* **44,** 242-248 (1973).
(21) A. W. Adamson, A model for micellar emulsions, *J. Colloid Interface Sci.,* **29,** 261-267 (1969).
(22) K. Shinoda and H. Kunieda, Conditions to produce so-called microemulsions: Factors to increase the mutual solubility of oil and water by solubilizer, *J. Colloid Interface Sci.* **42,** 381-387 (1973).

(23) G. Gillberg, H. Lehtinen, and S. Friberg, NMR and IR investigation of the conditions determining the stability of microemulsions, *J. Colloid Interface Sci.*, **33**, 40-53 (1970).
(24) E. Sjoblom and S. Friberg, Light-scattering and electron microscopy determination of association structures in W/O microemulsions, *J. Colloid Interface Sci.*, **67**, 16-30 (1978).
(25) S. Friberg and I. Burasczenska, Microemulsions in the water-potassium oleate-benzene system, *Progr. Colloid and Polymer Sci.*, **63**, 1-9 (1978).
(26) M. P. Shorr, P. Sharkey, and C. T. Rhodes, Dissolution of hydrocortisone, *J. Pharm. Sci.*, **61**, 1732-1735 (1972).
(27) B. W. Barry and D.I.D. El Eini, Solubilization of hydrocortisone, dexamethasone, testosterone and progresterone by long chain polyoxyethylene surfactants. *J. Pharm. Pharmac.*, **28**, 210-218 (1976).
(28.) B. R. Hajratwala and H. Taylor, Effect of non-ionic surfactants on the dissolution and solubility of hydrocortisone, *J. Pharm. Pharmac.*, **28**, 934-935 (1976).
(29) A. E. Allen and V. D. Gupta, Stability of hydrocortisone in polyethylene glycol ointment base, *J. Pharm. Sci.*, **63**, 107-109 (1974).
(30) V. K. Bansal, D. O. Shah, and J. P. O'Connell, Influence of alkyl chain length compatibility on microemulsion structure and solubilization, *J. Colloid Interface Sci.*, **75**, 462-475 (1980).
(31) K. E. Bennett, J. C. Hatfield, H. T. Davis, C. W. Macosko, and L. E. Scriven, Viscosity and Conductivity of Microemulsions, in *Microemulsions, et al.*, ed. I. D. Robb (Plenum Press, New York, 1982), pp 65-81.
(32) J. P. Camy *et al*, The Rheology of Crude Oil Dispersions, SPE paper 5299, Society of Petroleum Engineers of AIME, 1975.
(33) M. Lagues and C. Sautery, Percolation transition in water in oil microemulsions, electrical conductivity measurements, *J. Phys. Chem.*, **84**, 3503-3508 (1980).
(34) J. Lagourette, J. Peyrelasse, C. Boned, and M. Clausse, Percolative condition in microemulsion type systems, *Nature*, **281**, 60-62 (1979).
(35) S. H. Yalkowsky and T. J. Roseman, in "Techniques of Solubilization of Drugs," *Drugs and the Pharmaceutical Sciences*, **Vol. 12.**, ed. S. H. Yalkowsky (Marcel Dekker, Inc., 1981), p 129.
(36) D. O. Shah and R. S. Schechter, eds., *Improved Oil Recovery by Surfactant and Polymer Flooding* (Academic Press, New York, 1977).
(37) D. O. Shah, ed., *Surface Phenomena in Enhanced Oil Recovery* (Plenum Press, New York, 1981).
(39) D. O. Shah, The world of surface science, *Chem. Eng. Education*, Winter 1977, 14-48.
(39) S. I. Chou and D. O. Shah, The effect of H_2O and D_2O on colloidal properties of surfactant solutions and microemulsions, *J. Colloid Interface Sci.*, **80**, 49-54 (1981).
(40) C. Ramachandran, S. Vijayan, and D. O. Shah, Effect of salt on the structure of middle phase microemulsions using spin label technique, *J. Phys. Chem.*, **84**, 1561-1567 (1980).
(41) S. I. Chou and D. O. Shah, Dielectric relaxation of external microemulsions, *J. Phys. Chem.*, **85**, 1480-1485 (1981).
(42) D. O. Shah, in "Proceedings of the European Symposium on Enhanced Oil Recovery" (Elsevier Sequoia, S.A., 1981), pp 1-40.
(43) D. O. Shah, High resolution NMR studies on the structure of water in microemulsions and liquid crystals, *Ann. New York Acad. Sci.*, **204**, 125-133 (1973).