

DETERMINATION OF THE CMC OF SELECTED SURFACTANT
SOLUTIONS IN SYSTEMS CONTAINING CHLORAMPHENICOL

A.E. Aboutaleb, A.M. Sakr, and A. Abdelzaher
Department of Industrial Pharmacy, Faculty of Pharmacy,
Assiut University, Assiut, Egypt.

The solubility of Chloramphenicol was determined in solutions containing the following non-ionic surfactants: Tween 20, tween 40, tween 60, Emulgin C 1000, Emulgin C1500, Myrj 52, Myrj 53 and Myrj 59 together with cetrimide and sodium lauryl sulphate as representative examples for cationic and anionic surfactants. The solubilizing capacity of the different surfactant solutions above and below their CMC values were determined. It was concluded that all these surfactants when present in concentrations less than their CMC failed to enhance the solubility of chloramphenicol. The cationic and anionic surfactants showed the most significant increase in the drug solubility than the non-ionic surfactants above their CMC. The CMC values reported for the different classes of surfactants were found to be slightly different from literature reports.

The solubility measurement is frequently used for the determination of the CMC. This technique depends upon the fact that the actual solubilization of slightly soluble solute takes place only above CMC as below the latter no significant solubilization takes place¹. Non-ionic surfactants tend to form micelles at much lower concentration than their ionic counterparts²⁻⁴, due to the absence of electrostatic repulsion, thus methods other than solubility are not sufficiently sensitive for the CMC determination of the former. Techniques have been, therefore developed in an effort to overcome these difficulties⁵⁻⁶.

A photometric method⁷ has been reported for the determination of the CMC of the polyoxyethylene adducts in both aqueous and non-aqueous solutions, based on the formation of molecular complex

between iodine and non-ionic micelles. Becher⁸ has shown good agreement between the results of the previously mentioned method and the light scattering method with a range of commercial non-ionic detergents. Lucy and Philip⁹ determined the CMC of a series of polysorbates using a surface tension method. The CMC values obtained did not vary to any appreciable extent from those determined by other techniques.

Choules and Loh¹⁰ have determined also the CMC for aqueous solutions of polysorbates by interference refractometry method. It is well known that the surfactant molecular structure can affect the micellar size^{11,12}. Generally the CMC decreases as the hydrocarbon chain length increases for the same head group as the polyoxyethylene chain length. The purpose of this work is to determine the CMC values of some selected surfactant solutions by the solubility technique and to compare them with literature reports.

EXPERIMENTAL

Materials

The non-ionic surfactants used in this study were Tween 20, Tween 40, Tween 60 and Tween 80^a, Emulgin series which include Emulgin^c 1000 and Emulgin^c 1500^d Myrj series especially Myrj 52, Myrj 53 and Myrj 59^a were used. Certrimide and sodium lauryl sulphate^c were also employed as representative example for cationic and anionic surfactants respectively. Chloramphenicol^d was analytical grade.

Determination of the critical micellar concentration:-

The solubility method was used for the determination of CMC values of the different surfactant solutions. Stock solutions (5% w/v) of the previously mentioned surfactants in distilled water were prepared. Serial dilutions for each surfactant solution from

-
- a) Atlas Chemical Ind. Del. U.S.A.
 - b) Henkel International, Dusseldorf, West Germany.
 - c) B.D.H. pools, U.K
 - d) El-Nasr Company, Egypt.

0.001% to 1% w/v for non-ionic or 0.01% to 5% w/v for cationic and anionic surfactants which represent concentrations above and below the expected CMC values were used. From each diluted solution, 10 ml was placed in 15 ml stoppered tubes in a constant temperature water bath, thermostatically controlled at $(25^{\circ} \pm 1)$. Excess of solid chloramphenicol (100 mg) was added to each tube and the solutions were equilibrated by shaking for 14 days.

The tubes were then centrifuged and reequilibrated for further 24 hours. Samples were withdrawn and appropriately diluted with distilled water. Chloramphenicol was determined spectrophotometrically at 275 nm in the supernatant surfactant solution using distilled water as a blank. The presence of surfactants, at this dilution range did not interfere with the assay of chloramphenicol or exhibit any shift in the wave length of its maximum absorbance.

RESULTS AND DISCUSSION

Choulis and Lucy¹¹ have determined the CMC of polysorbates by interference refractometry and surface tension methods. In the present work, the CMC of polysorbates, Emulgins, Myrj's, cetrimide and sodium lauryl sulphate were determined by the solubility technique. The solubility of chloramphenicol in the different surfactant solutions, below and above their expected CMC values were determined at 25° as shown in Figures 1-3 and tables 1-3. It was found that the solubility of chloramphenicol slightly affected at low concentrations of the surfactant solutions. On the other hand, the solubility begins to increase after reaching certain concentration which is characteristic for each surfactant. This value is considered as the CMC value at this specific temperature. The CMC can be easily obtained from the break in solubility curves for chloramphenicol as shown in Figures 1-3.

The values of CMC determined by this method were slightly lower than those reported by other techniques as shown in Table 4. This may be due to the presence of solubilizate, but, this lowering in the CMC values was not great in the case of systems containing chloramphenicol. Slight increase in solubility of chloramphenicol appears just below CMC for the different surfactant solutions which may be due to the limited association concentration i. e. formation of micelles of a limited or small aggregation numbers.

The lower CMC values obtained may be due to the effect of chloramphenicol on the process of micellization as it is known that most of solutes can induce micelle formation consequently the CMC can be formed at relatively smaller concentration⁸ Furthermore, these systems were considered to be heterodispersed systems and impurities usually present in commercial surfactants as unlinked ethylene oxide or compounds with shorter ethylene oxide chain lengths can even form dip at the CMC values. Non-ionic surfactants form micelles at lower concentration than ionic ones for the same hydrocarbon chain length due to lack of electrical work in transferring monomers into a micelle for the former class of materials. Consequently, non-ionic surfactants considered to be more efficient solubilizers than cationic and anionic surfactants as shown in Figures 1-3 .

The CMC values differ also by variation in surfactant molecular structure in a homologous series. As the hydrocarbon chain length increases for the same polyoxyethylene chain, the CMC value decreases and the micelle size increases due to increase in aggregation number as the driving force of micellization will be greater than for short ones. This is well illustrated in Figure 1 and Table 1, for the polysorbate series, as the hydrocarbon chain length increases for the same polyoxyethylene chain length, the CMC values were found to be markedly decreased. Thus the CMC of Tween 80 was found to be lower than Tween 60, 40 or 20 respectively. On the contrary, as the polyoxyethylene chain length increases for a homologous series containing the same hydrocarbon chain length, the CMC value was found to increase markedly. This is best illustrated in Figure 2 and Table 2 for the Emulgins and Myrj series. It can be noticed that the CMC value of Myrj 59 was higher than Myrj 53 and 52 respectively. This was also the case for Emulgin C1500 and Emulgin C1000 as the value of the latter was lower than the former, for the same reason.

From Figure 3 and Table 3, it is clear that cetrimide has lower CMC value than sodium lauryl sulphate, because the former has less electrical repulsion, and consequently needs less electrical work for transferring monomers into micelles than the latter

Table (1) : Solubility of Chloramphenicol in Tween Solutions
Below and Above their CMC at 25°C.

Log (Surfactant % w/v x 10 ⁶)	Log (Chloramphenicol Solubilized % w/v x 10 ⁶)			
	Tween 20	Tween 40	Tween 60	Tween 80
2.69	5.584	5.589	5.595	5.600
3.00	5.584	5.589	5.595	5.600
3.30	5.584	5.589	5.595	5.509
3.60	5.584	5.589	5.604	5.617
3.69	5.584	5.601	5.607	5.620
4.00	5.595	5.611	5.617	5.628
4.30	5.606	5.621	5.626	5.637
4.69	5.620	5.633	5.639	5.648
5.00	5.631	5.643	5.648	5.657
6.00	5.668	5.675	5.680	5.685

Table (2): Solubility of Chloramphenicol in Emulgin and Myrj Solutions below and above their CMC at 25°

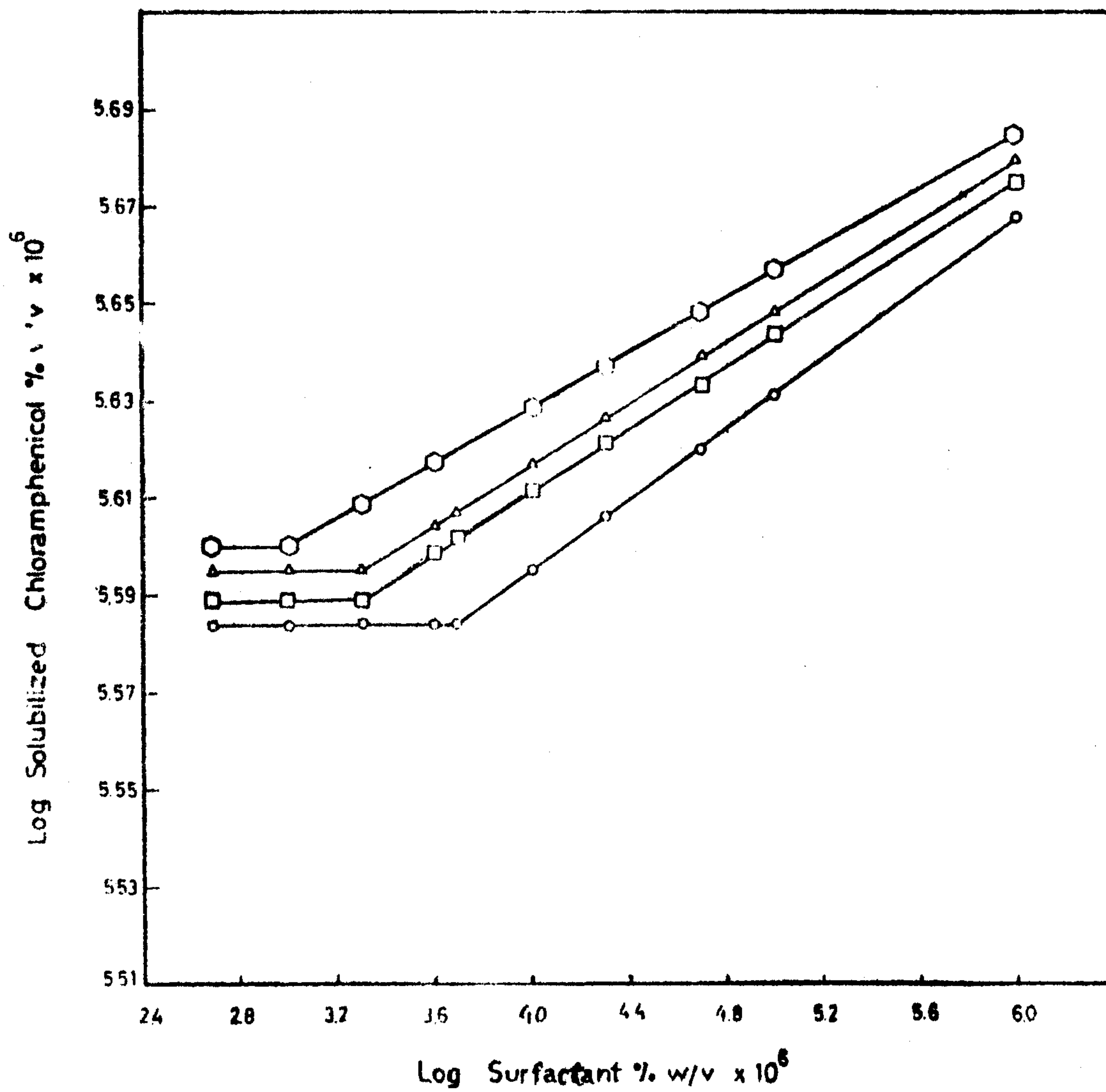
Log (Surfactant % w/v $\times 10^6$)	Log (Chloramphenicol Solubility % w/v $\times 10^6$)				
	Emulgin C ₁₀₀₀	Emulgin C ₁₅₀₀	Myrj 52	Myrj 53	Myrj 59
2.69	5.605	5.603	5.597	5.596	5.587
3.00	5.614	5.603	5.698	5.596	5.587
3.30	5.622	5.611	5.598	5.596	5.587
3.60	5.631	5.620	5.598	5.596	5.587
3.69	5.633	5.623	5.598	5.598	5.587
4.00	5.642	5.631	5.606	5.596	5.587
4.3	5.651	5.640	5.613	5.603	5.587
4.69	5.662	5.651	5.621	5.612	5.594
5.00	5.670	5.660	5.628	5.618	5.600
6.00	5.699	5.689	5.649	5.640	5.619

Table (3): Solubility of Chloramphenicol in Cetrимide and Sod. Lauryl Sulphate Solutions Below and above their CMC at 25°C.

Log (Surfactant % w/v $\times 10^6$)	Log (Chloramphenicol Solubility % w/v $\times 10^6$)	
	Sod. Lauryl Sulphate	Cetrимide
2.69	5.589	5.582
3.00	5.589	5.582
3.30	5.589	5.582
3.60	5.589	5.582
3.69	5.589	5.582
4.00	5.589	5.582
4.30	5.589	5.582
4.69	5.589	5.602
5.00	5.589	5.617
6.00	5.762	5.870

Table (4): Comparison between CMC values of different Surfactant Solutions Obtained from Solubility Measurements and those Obtained by other Methods at 25°C.

<i>Surfactant</i>	<i>CMC values g% w/v obtained by the Solubility methods</i>	<i>CMC values g% w/v obtained by other methods</i>
Tween 20	0.0048	0.006
Tween 40	0.0019	0.0029
Tween 60	0.0019	0.0027
Tween 80	0.0010	0.0013
Emulgin C ₁₀₀₀	0.00048	0.0011
Emulgin C ₁₅₀₀	0.0010	0.0012
Myrj 52	0.0048	0.011
Myrj 53	0.010	0.014
* Myrj 59	0.0199	0.02
Cetrimide	0.0199	0.067
Sod. lauryl Sulphate	0.100	0.29



Fig(1) Solubility of Chloramphenicol in Tweens solutions below and above CMC at 25°

Key: ○ Tween 20. □ Tween 40. △ Tween 60. ● Tween 80.

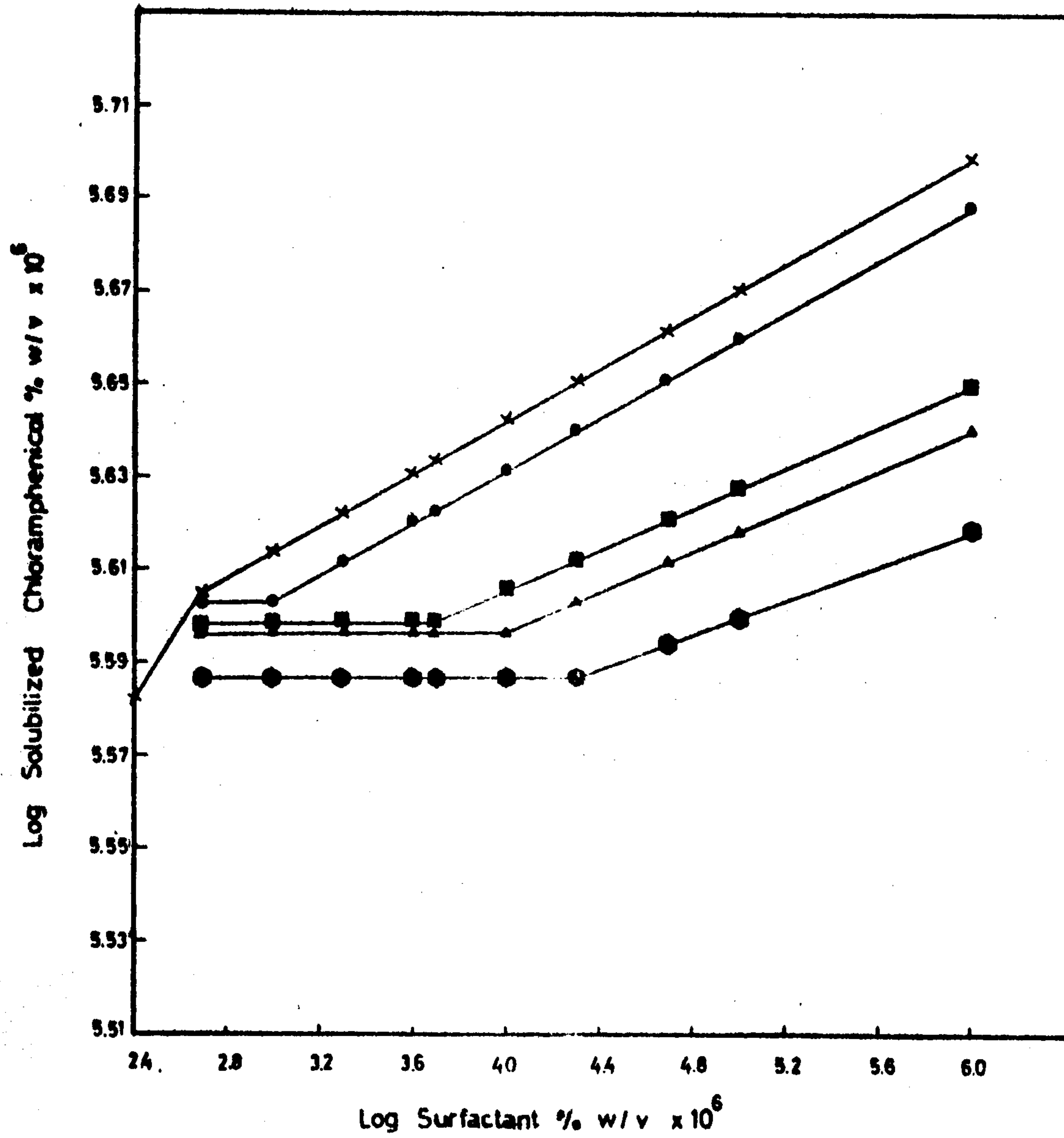


Fig.(2) Solubility of Chloramphenicol in Emulgin and Myrj solutions below and above CMC at 25°.

Key: x Emulgin C1000. o Emulgin C1500. ■ Myrj 52.
 ▲ Myrj 53. ● Myrj 59.

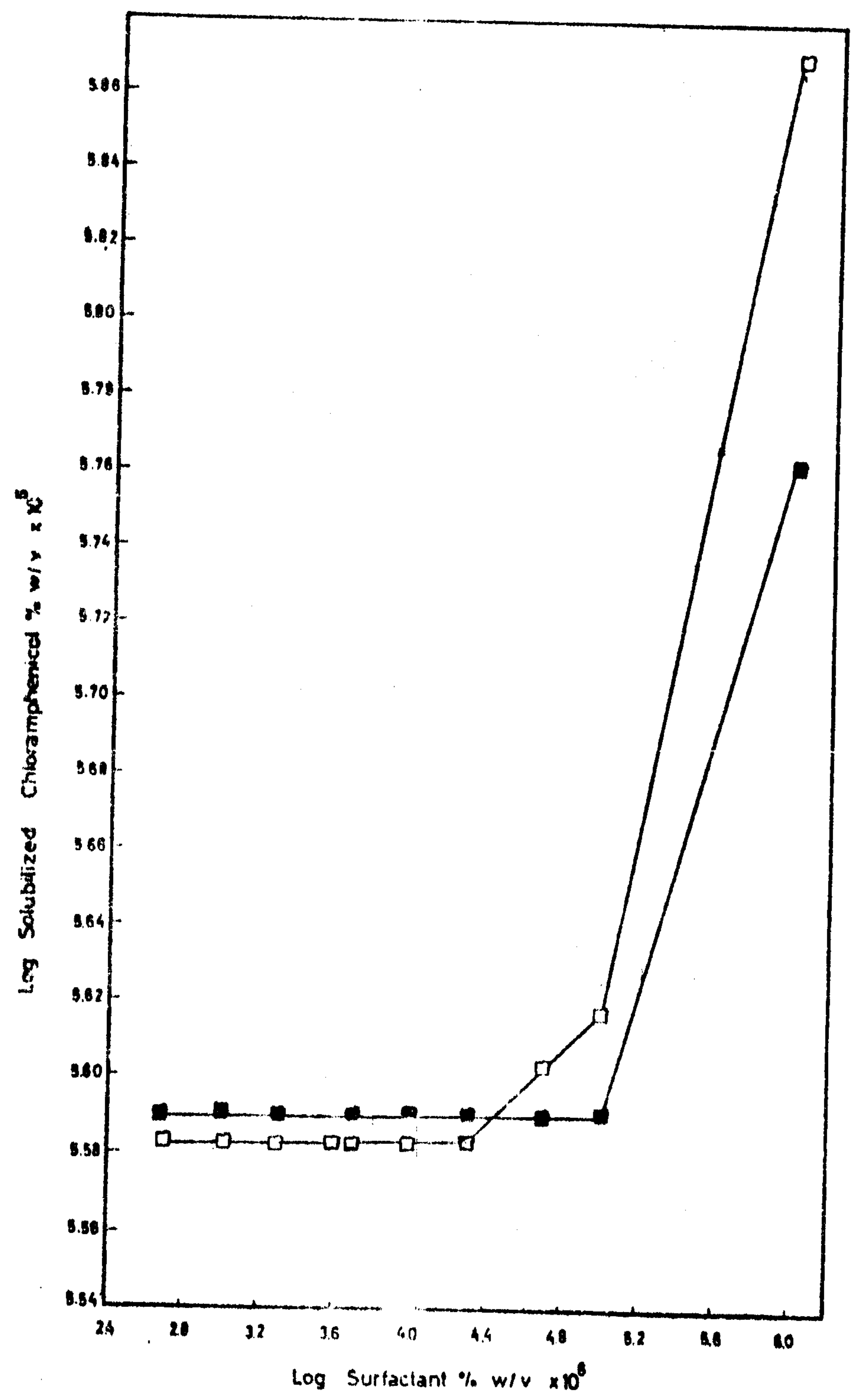


Fig.(3) Solubility of Chloramphenicol in anionic and cationic Surfactant solutions below and above CMC at 25°.
Key: □ Cetrimide ■ Sod. Lauryl Sulphate.

REFERENCES

- 1) Mukerjee, P. and Mysels, K., *J. Am. Chem. Soc.*, 77, 2937 (1955) .
- 2) Nakagawa, T., *Shionogi Kenkyusho, Nempo*, 8, 824 (1958).
Bury, C. R. and Browning, J., *Trans Farady Soc.*, 49, 209 (1953).
- 3) Cohen, M., *Mem. Services, Chim. etat.*, 37, 85 (1952).
- 4) Nakagawa, T., Kuriyama, K., Inaba, M. and Tori, K., J., *Chem. Soc. Japan*, 77, 1563 (1956).
- 6) Weil, J.K., and Stirtion, A.J., *J. Phys. Chem.*, 60, 899 (1956).
- 7) Ross, S. and Olivier, J.P., *ibid*, 63, 1971 (1959).
- 8) Becher, P. *ibid.*, 63, 1675 (1959)
- 9) Lucy, S.C. and Philip, F.S., *J. Pharm. Sci.*, 63, 136 (1974)
- 10) Choulis, N. H. and Loh, L. H. , *Canad. J. Pharm. Sci.*, 6, 63 (1971).
- 11) Choulis, N. H., *ibid*, 5, 24 (1970) .
- 12) Beckett A. H., Kirk, G., and Virji, A. S., *J. Pharm. Pharmacol.*, 19, 71 (1967).

تعيين التركيزات الحرجة لتكوين الشباك في محاليل منشطات سطح منتخبة في انظمة تحتوى

على الكلوراينيكول

احمد السيد ابوطالب - احمد عادل صقر - على عبد الظاهر

قسم الصيدلة الصناعية - كلية الصيدلة - جامعة اسيوط

تم تعيين اذابة الكلوراينيكول في محاليل منشطات السطح الغير متأينة وهى التوين ٢٠ ٤٠٥ ٦٠٥
والايجين س ١٠٠٠ وس ١٥٠٠ والميرج ٥٢ ٥٩٠ وكذلك محاليل منشطات موجبة الشحنة وسالبة الشحنة
وقد وجد ان درجة الاذابة لمحلول كل منعط تختلف كثيرا حسب التركيزات المستخدمة قبل وبعد التركيزات
اللازمة لتكوين الشباك وقد استنتج ان ذوبان الكلوراينيكول لا يتأثر كثيرا قبل التركيزات الحرجة لمحاليل
المنشطات المختلفة وقد لوحظ ان المنشطات موجبة الشحنة تعطى درجة اذابة اكر من سالبة الشحنة والغير
متأينة وذلك بعد التركيزات الحرجة لتكوين الشباك وقد قورنت التركيزات الحرجة لتكوين الشباك المعينة بهذه
الطريقة بتلك المعينة بطرق اخرى فوجدت انها تختلف قليلا عنها مما يعطى هذه الطريقة اهمية نظرا -
اهميتها وعدم تأثير الكلوراينيكول على التركيزات الحرجة للمنشطات المختلفة .