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APPLICATION OF DIALYSIS UNDER PRESSURE FOR INVESTIGATING THE INTERACTION BETWEEN CHLOR-AMPHENICOL AND NON-IONIC SURFACTANTS

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Ultrafiltration technique was applied for investigating undersaturated systems containing chloramphenicol using Diaflo membrane UM 05. This durg was solubilized by a series of non-ionic surfactants which include Tween 20, Tween 40, Tween 60, Tween 80, Emulgin C 1000, Emulgin C 1500, Myrj 52, Myrj 53 and Myrj 59. At two different tempertatures.

It was found that the amount of chloramphenicol bound to the micelles as calculated from the ultrafiltration experiments was greater for Emulgin C 1000, than Emulgin C 1500 On the other hand the binding capacity of the different Tweens for chloramphenicol can be arranged as follows: Tween 80> Tween 40> Tween 60> Tween 20. For Myrj series, Myrj 52 was found to be greater than Myrj 53 and both were higher than Myrj 59.

Ultrafiltration, is a process of separation, whereby a solution containing two solutes of greatly different molecular dimensions are separated by forcing the solute of lower molecular dimension under a hydraulic pressure gradient to flow through a suitable membrane which makes retention to the solute of the higher colloidal dimension. Aboutaleb[1] used Diaflo membranes UM 05 and pellicon 1000 ultrafiltration membranes for investigating solubilized systems containing benzoic acid and salicylamide. Shimamoto and Ogawa[2] made a comprehensive study on the binding of preservatives by non-ionic surfactants in different pharmaceutical formulations using this technique. It was also reported that[3] the antimicrobial activity of preservatives incorporated in oil-in-water emulsion systems was mainly controlled by the concentration of free species.

In the present work, ultrafiltration technique was used for investigating the mechanism of interaction between chloramphenicol and the different non-ionic mecelles.

Furthermore, the activity or the amount of chloramphenicol free in solutions can be estimated easily for the different systems and within a short time.

EXPERIMENTAL

Materials:

Chloramphenicol[1] was of analytical grade, non-ionic surfactants:

Tweens[2] : Polyoxyethylene sorbitan monolaurate(Tween 20), Polyoxyethylene sorbitan monostearate (Tween 40), Polyoxyethylene sorbitan monopalmitate(Tween 60) and polyoxyethylene sorbitan monoleate (tween 80).

Myrjs[2]: Polyoxyl 40 stearate (Myrj 52), Polyoxyl 50 stearate (myrj 53) and polyoxyl 100 stearate (Myrj 59).

Emulgins[3]: Cetyl stearyl alcohol with 20 ethylene oxide units

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1- El-Nasr chemical Co. Egypt

2- Atlas chemical Industries Delaware U.S.A.

3- Henkel International, Desseldorf West Germany.

(Emulgin ^{C}1000) and cetyl stearyl alcohol with 30 ethylene oxide units (Emulgin^{C}1500). The number between brackets denotes the number of ethylene oxide units present in the surfactant.

Apparatus

Amicon ultrafiltration cell[4] model C_{12} of capacity 10 ml

Diaflo membrane UM 05[2]

Method used for studying the interaction between chloramphenicol and non-ionic surfactant solutions:

The semi-continuous method was used for investigating the systems containing chloramphenicol in 2, and 5% w/v surfactant solutions. A pressure of 60 lb/in^{-2} was applied. Six fractions of the effluents, each of 5 ml, were collected in two portions and each fraction was then replaced by 5 ml distilled water. Chloramphenicol was analyzed in the second portion of each fraction spectrophotometrically by reading the absorbance at 278 nm. after appropiate dilution with distilled water.

The results obtained were plotted as-log C_n/C_o against(n-1) as shown in Tables 1, 2 and Figures 1-4.

RESULTS AND DISCUSSION

The ultrafiltration semicontinous method was adopted for the determination of the degree of binding of chlormphenicol to different non-ionic surfactant micelles. The results obtained were plotted according to a model proposed by a number of workers[4,5], according to the following equation:

$$\log C_n/C_o = \log F + (n-1)\log\left(1-\frac{F_v}{V}\right)$$

4- Amicon corporation, Mascachusetts, U.S.A.

Where C_o is the original solute concentration, C_n is the concentration of the solute in the effluent n, V is the initial volume of solution in the cell, F is the fraction free of the solute, V is the volume of each effluent and n is the number of effluents collected.

A plot of $- \log C_n / C_o$ against (n-1) will give a straight line of slope $(1- \frac{F_v}{V})$ and intercept equal log F.

This treatment is suitable for binding of reversible type. The value of F, which is the faction free, can then, be obtained from both slope and intercept from which the amount free in solution, can be calulated. Thus, the amount of Chloramphenicol bound to different non-ionic surfactant micelles can, then be determined.

On using ultrafiltration technique for studying the interaction between chloramphenicol and non-ionic surfactant solutions, it is important to determine the degree of binding of chloramphenicol alone in absence of surfactant to the ultrafiltration membrane used in the present work, (Diaflo UM05) as a modern type of diffusive membranes. This was determined by performing ultrafiltration experiments using a known intial concentration of chloramphenicol in water. The degree of binding was followed by analyzing the effluents collected[5]

It was found that chloramphenicol concentration in the first effluent was nearly equal to the initial concentration used. This means that Diaflo UM05 membrane is freely permeable to chloramphenicol and insignificant amount of chloramphenicol was bound to the Diaflo UM05 membrane.

On performing the experiments using different concentrations of chloramphenicol in the different non-ionic surfactant solutions and calculating the results as mentioned before, a relationship was obtained between the intial concentration of the solute in the ultrafiltration cell and the filtrate using this semi-continuous method. Consequently, the fraction free of the solute in the nonmicellar aqueous phase can be estimated, assuming that the latter was constant as proposed in the previously mentioned model. This is equivalent to assuming a partition law relationship for the distribution of the solute between the water and micellar pseudo-phase. It can be noticed from Figures 1-4 and Table 1,2 that the data when plotted in the appropriate manner gave straight lines as required by this theoretical treatment, confirming the partition law assumption. Also, the distribution coefficient calculated using the values of F obtained was not affected by changing either Chloramphenicol or surfactant concentration. This gives further support to partition model of solubilization. Again, the fraction free F obtained from slopes and intercepts of the straight lines were nearly the same. This also reveals the validity of this theoretical treatment which confirms this model.

It may be concluded that the results obtained from the ultrafiltration technique for the undersaturted systems containing chloramphenicol in the different non-ionic surfactants used provide further support to the pseudo-two phase model of solubilization proposed by McBain and Hutchinson[6] Furthermore, the ultrafiltration technique is of particular interest since it can be used for estimating the degree of interaction between chloramphenicol and non-ionic surfactants within a shorter time.

Moreover, the availability (the amount free) of chloramphenicol from the solutions containing these non-ionic surfactants can also be obtained even at very low concentration of chloramphenicol.

Table 1: Results of Ultrafiltration experiments using chloramphenicol in 2% w/v surfactant solutions at 32 ± 2°.

Effluent number	$-\log {}^{C_n}/{}_{C_o}$ values for the effluents of different surfactant solutions								
n	Tween 20	Tween 40	Tween 60	Tween 80	Emulgin C_{1000}	Emulgin C_{1500}	Myrj 52	Myrj 53	Myrj 59
1	0.28	0.33	0.38	0.41	0.42	0.39	0.38	0.36	0.32
2	0.36	0.42	0.47	0.50	0.53	0.50	0.48	0.46	0.41
3	0.46	0.53	0.58	0.60	0.63	0.61	0.57	0.55	0.51
4	0.52	0.64	0.69	0.70	0.715	0.715	0.67	0.65	0.61
5	0.66	0.75	0.80	0.81	0.80	0.83	0.77	0.75	0.7
6	0.74	0.84	0.88	0.91	0.91	0.92	0.87	0.84	0.78

C_n : Concentration of chloramphenicol % w/v in the effluent.

C_o : Initial concentration of chloramphenicol % w/v.

Table (2): Results of ultrafiltration experiments using chloramphenicol in 5% w/v surfactant solution at 32 ± 2°

Effluent number n	$-\log {}^{C}n/{}^{C}o$ values for the effluent of different surfactant solutions								
	Tween 20	Tween 40	Tween 60	Tween 80	Emulgin C_{1000}	Emulgin C_{1500}	Myrj 52	Myrj 53	Myrj 59
1	0.43	0.61	0.55	0.66	0.68	0.64	0.64	0.57	0.47
2	0.47	0.70	0.61	0.75	0.73	0.72	0.68	0.63	0.53
3	0.52	0.78	0.69	0.87	0.79	0.78	0.74	0.68	0.58
4	0.57	0.85	0.76	0.92	0.84	0.83	0.80	0.75	0.64
5	0.62	0.92	0.83	1.0	0.88	0.89	0.85	0.80	0.70
6	0.67	1.00	0.90	1.09	0.93	0.95	0.90	0.85	0.75

C_n : Concentration of chloramphenicol % w/v in the efflient.

C_o: Initial concentration of chloramphenicol % w/v.

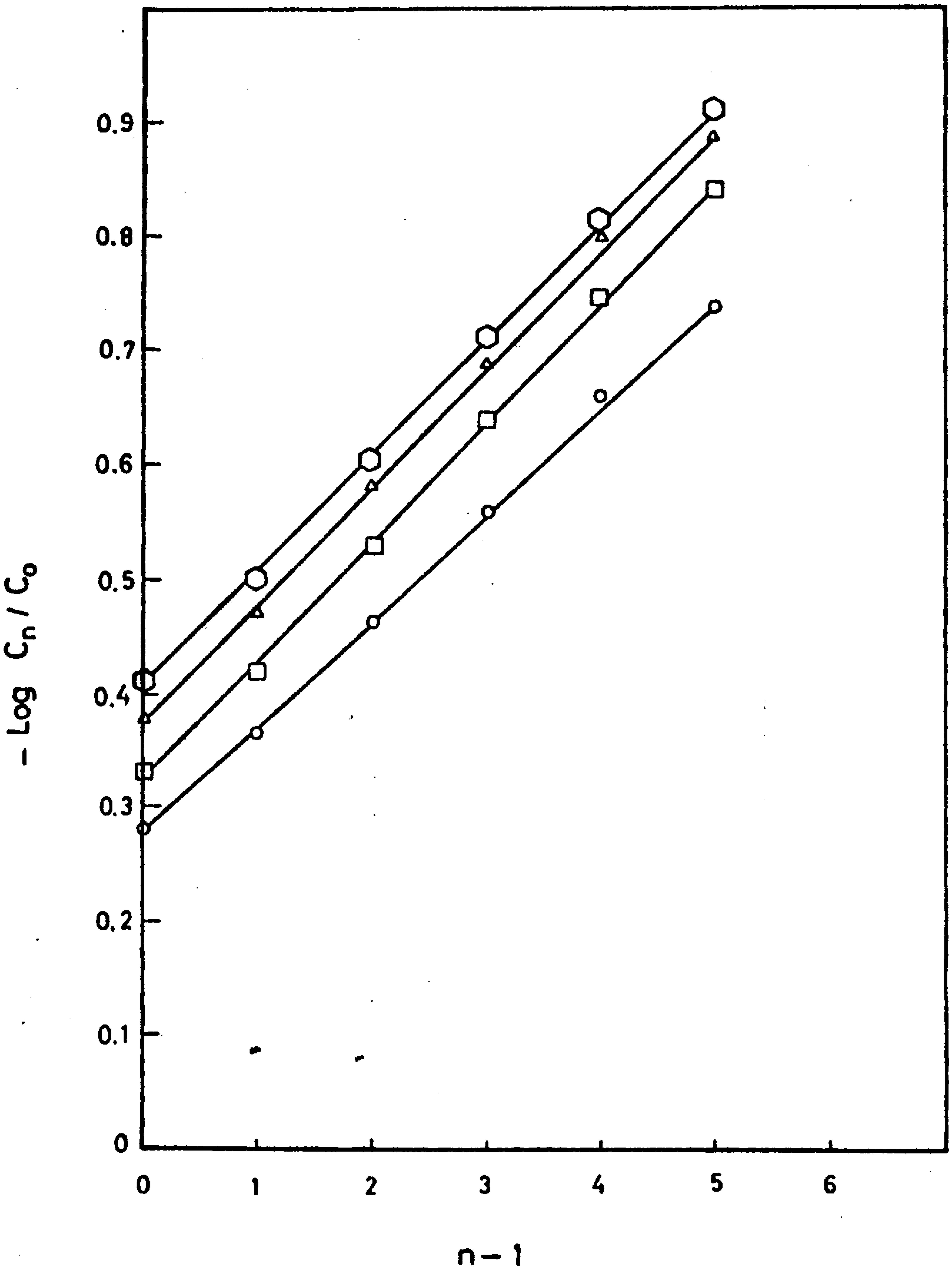

Fig.(1) Ultrafiltration experiments using different concentrations of Chloramphenicol in 2 % w/v Tween solutions .

Key: ○ Tween 80. △ Tween 60. □ Tween 40. o Tween :

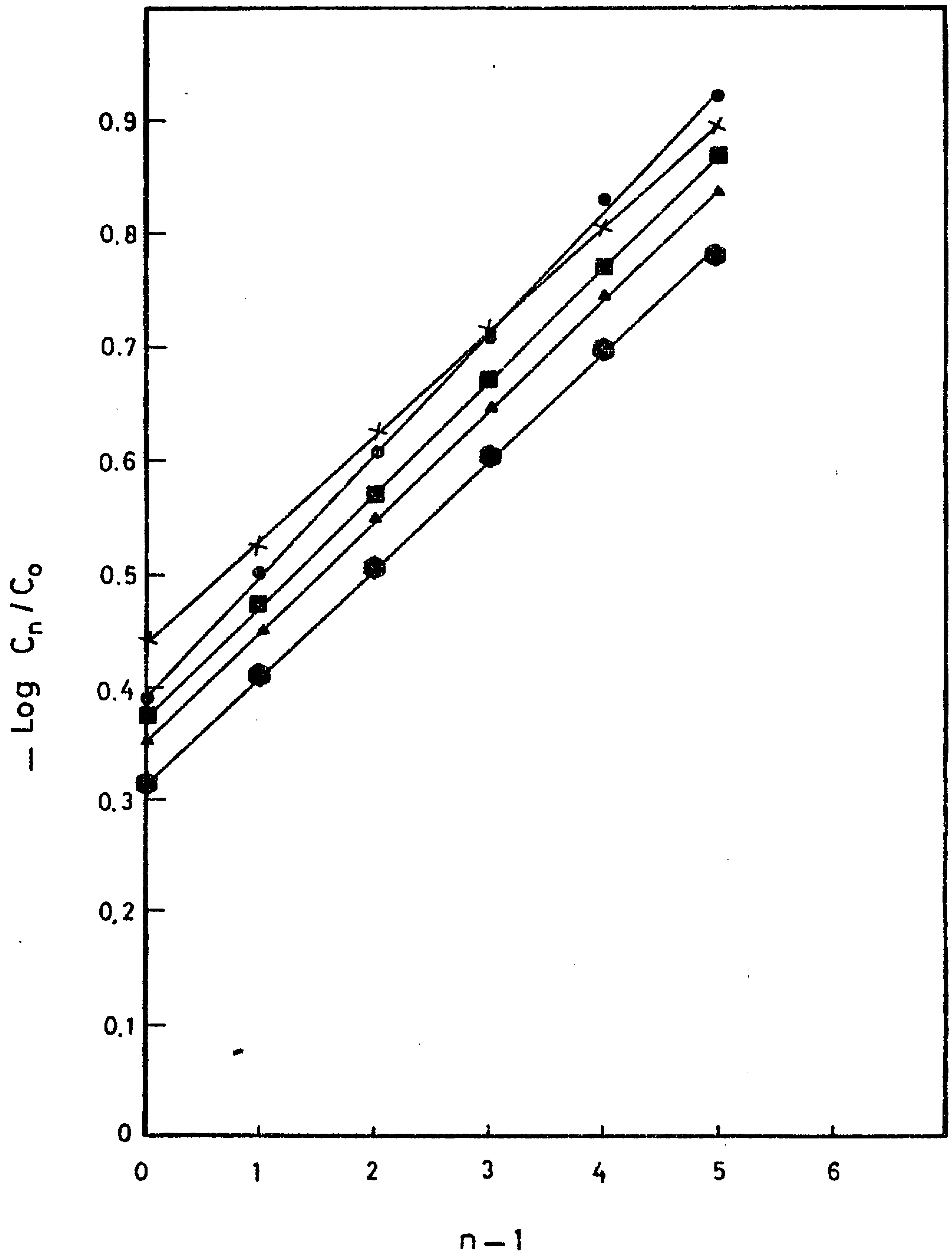

Fig.(2) Ultrafiltration experiments using different concentrations of Chloramphenicol in 2% w/v Myrj and Emulgin solutions.

Key: × Emulgin C1000. • Emulgin C1500. ■ Myrj 52. ▲ Myrj 53. ⬣ Myrj 59.

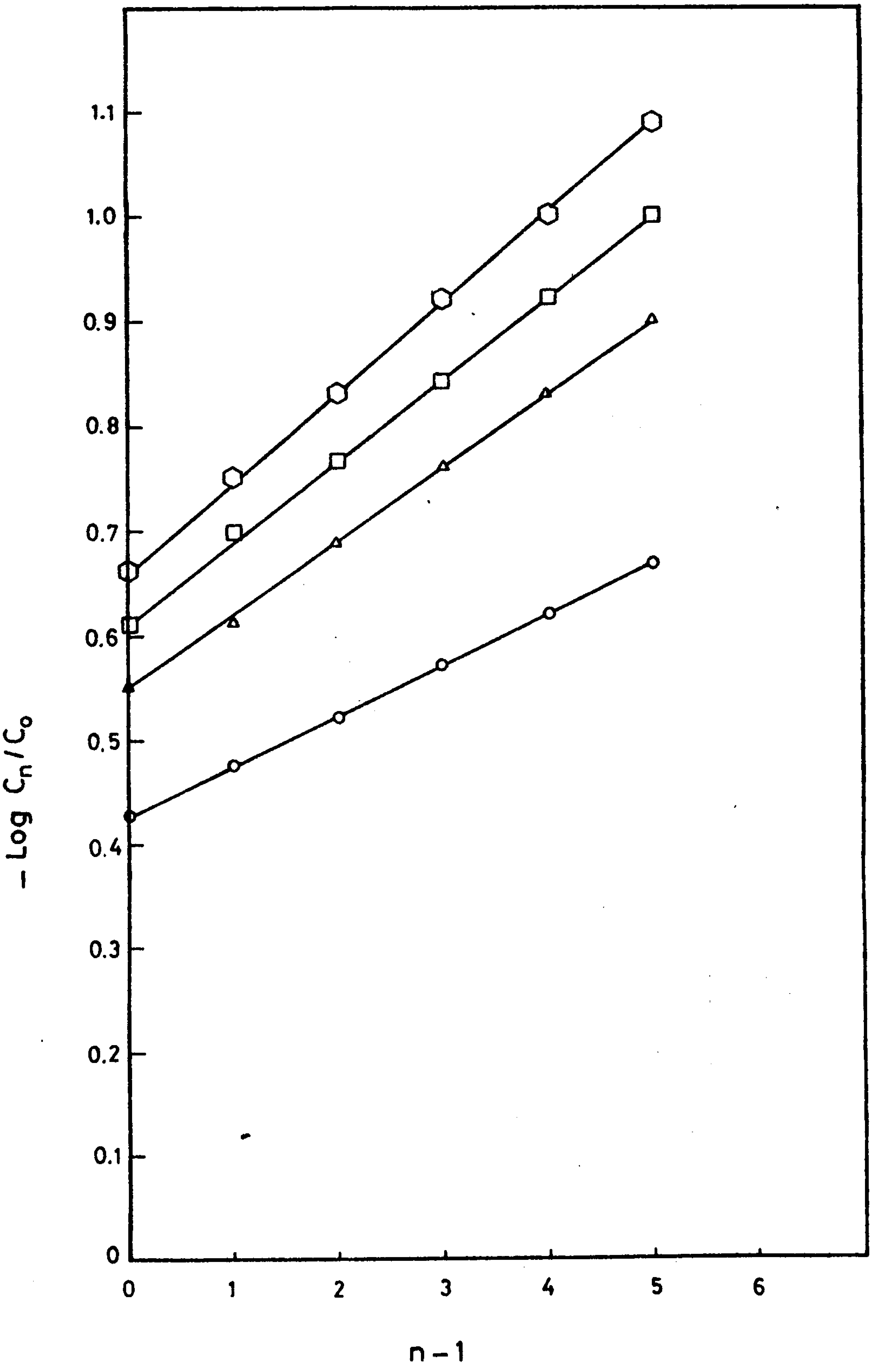

Fig.(3) Ultrafiltration experiments using different concentrations of Chloramphenicol in 5% w/v Tween solutions.

Key: The same as Fig.(1).

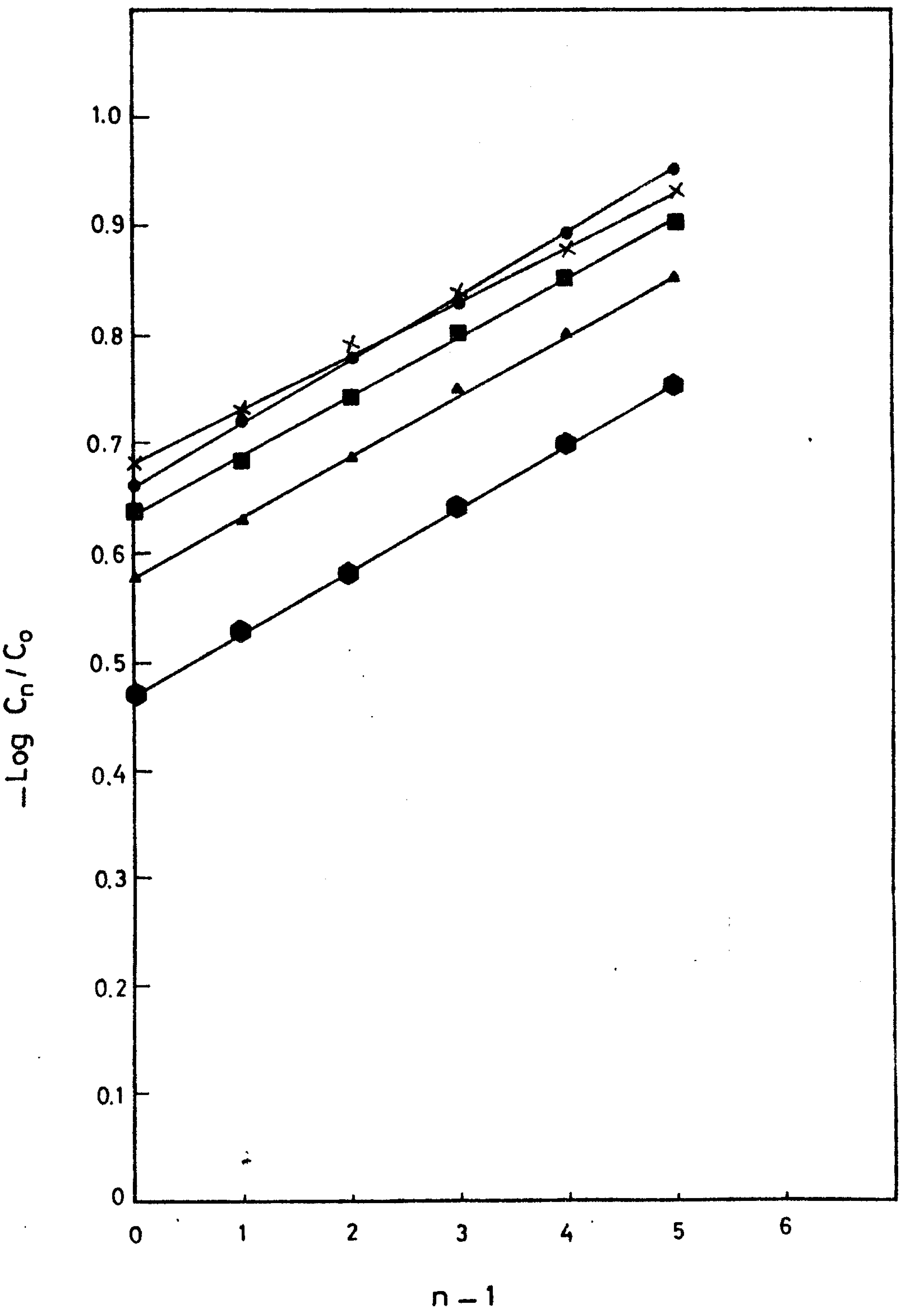

Fig.(4) Ultrafiltration experiments using different concentrations of Chloramphenicol in 5% w/v Myrj and Emulgin solutions .

Key: The same as Fig.(2).

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تطبيق الترشيح تحت ضغط مرتفع لدراسة التفاعل بين الكلورامفينكول ومنشطات السطح غير المتأينة

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استخدمت طريقة الترشيح تحت ضغط مرتفع لدراسة النظم تحت المشبعة التي تحتوى على الكلورامفينكول مذابا فى منشطات السطح غير المتأينة باستخدام غشاء الديافلويوم او ٥ أذيب هذا العقار باستخدام منشطات السطح غير المتأينة والتى تشمل : التوين ٢٠ ، التوين ٤٠ ، التوين ٦٠ ، التوين ٨٠ ، الاملجين س ١٠٠٠ ، الاملجين س ١٥٠٠ ، الميرج ٥٢ ، الميرج ٥٣ ، الميرج ٥٩ .

ولقد وجد أن كمية الكلورامفينكول المذابة فى الشباك فى درجتى حرارة مختلفتين كما حسبت من تجارب الترشيح تحت ضغط مرتفع ، اكبر فى الاملجين س ١٠٠٠ من الاملجين س ١٥٠٠ ومن الناحية مقدره التوينات على اذابة الكلورامفينكول رتبت كالتالى : توين ٨٠ اكبر من توين ٤٠ اكبر من توين ٦٠ اكبر من توين ٢٠ .

اما سلسلة الميرج فقط وجد ان اكبر مذيب للكلورامفينكول هو ميرج ٥٢ واصغرهم هو ميرج ٥٩ .