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KINETICS OF ASPRIN HYDROLYSIS IN AQUEOUS SOLUTIONS OF SURFACTANTS III: SODIUM LAURYL SULFATE.

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ABSTRACT

The hydrolysis of aspirin solution at a variety of pH values and in presence of increasing concentrations of sodium lauryl sulfate (SLS) was investigated at 35°C. The hydrolysis followed first order kinetics. The results indicate that the presence of sodium lauryl sulfate results in a protection of aspirin against hydrolysis and the degree of protection was found to be dependent on the surfactant concentration. This finding was explained on the basis that as the surfactant concentration was increased, aspirin was distributed in a favour of the micellar phase and the amount of aspirin exists in the true aqueous phase, which is susceptible to hydrolysis, is reduced. Also, the data revealed that the presence of sodium lauryl sulfate did not alter the optimum pH value for the stability of aspirin solution which was found to be 2.4.

INTRODUCTION

When a slightly water-soluble compound is solubilized by a surface active agent, it is a widely adopted assumption that the solubilizate is distributed between the micellar and the aqueous phases. Consequently, when a surface active agent is added in a con-

centration above its CMC, to the aqueous solution of the hydrolytic drugs, it may be expected that a part of the drug molecules will move towards the hydrophobic moiety of the micelles. Accordingly, the hydrolytic process will be retarded or prevented and the solution of the drug will be stabilized.

Mitchel[1] studied the effects of sodium lauryl sulfate (SLS) and cetrimide on the alkaline hydrolysis of propyl benzoate and he compared the results with that obtained previously in cetomacrogol aqueous solutions[2]. Generally, he found that the hydrolysis rate of the ester decreased with increase in the surfactant concentration. Also, he investigated the effect of cetrimide on the alkaline hydrolysis of ethyl benzoate, diethylphthalate and aqueous solutions of benzocaine[3]. He concluded that increasing the concentration of cetrimide alters the distribution of ester in favour of the micelles and the rate of the hydrolysis decreased..

The effect of pH, temperature and ionic strength on the degradation of phenobarbital, in a solubilized system containing sodium lauryl sulfate was studied by Khalil et al.[4]. They found that the surfactant had a stabilizing effect as compared with the control. However, this effect of the surfactant was found to be less than that produced by the non-ionic surfactants.

Kassem et al[5] studied the effect of non-ionic surfactants on the stability and in vitro availability of chloramphenicol in solution. They found that the stability increased with increasing the surfactants concentration. Contrarily, the in vitro availability was markedly reduced at a relatively high surfactant concentration.

Recently, Ismail and Simonelli investigated the hydrolysis of aspirin in polysorbates solutions at different pH values[6] as well as the effect of different concentrations of cetrimide on the

hydrolysis rate of aspirin[7]. Generally, they found that the rate of aspirin hydrolysis decreased with increasing the surfactant concentration.

The present investigation is concerned with the determination of aspirin stability in a wide range of pH values from pH 1 to pH 9 and in presence of variable concentrations of sodium lauryl sulfate. This surfactant was selected to find out the effect of attractive and repelling forces on the stability of aspirin solution. Aspirin was selected as a model drug representing the compounds having an ester group and susceptible to be hydrolyzed by hydronium or hydroxyl ions. Also, aspirin was chosen due to its ease of assay to follow its decomposition.

EXPERIMENTAL

Materials:

Aspirin[a], Sodium lauryl sulfate (SLS)[b], Hydrochloric acid[c], Potassium chloride[d], Sodium hydroxide[c], Citric acid[e], Sodium phosphate dibasic[e], Sodium chloride[e], pure grades of Glycine and Ferric nitrate.

Apparatus:

1- Constant temperature water-bath held at 35 C°.

2- Self-recording double beam spectrophotometer (Pye Unicam).

3- Digital pH meter (Pye Unicam).

Methods:

Reagent Solution:

The hydrolysis of aspirin was followed by the determination of the concentration of salicylic acid, as each molecule of aspirin yields one molecule of

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a- USP grade.
b- BDH, England.
c- Prolabo.
d- Sigma Chem. Co., USA.
e- El-Nasr Pharm Co., Egypt.

salicylic acid. The concentration of salicylic acid was measured colormetrically at 530 nm. The colour reagent used contains in each 100 ml of aqueous solution 4 g of ferric nitrate, 4 g mercuric chloride and 12 ml of N H Cl[8].

Buffer Solutions[9]:

The buffer solutions used for determining the pH profile of aspirin degradation were: pH range 1 - 1.8, Clark and Lubs, K Cl/ H Cl, pH range 2.4 - 7, McIlvaine, disodium phosphate and citric acid; pH range 8 - 9, Sørensen, glycine/ Na OH.

Stability Study:

Solutions of aspirin (1 mg/ml) in a suitable buffer at the selected pH value either in absence or presence of increasing concentrations of SLS, were prepared. The ionic strength of each solution was adjusted, with sodium chloride to 0.5. Portions of these solutions were placed in a thermostated water bath at 35°C. The temperature of the tested aspirin solution was followed until it reached 35°C ± 0.2. The time was recorded and considered as the initial one. The concentration of salicylic acid exists at the starting time and that formed at suitable time intervals was estimated by pipetting 2 ml of aspirin solution into 17 ml of pH 2.4 buffer solution, which containing 8% benzalkonium chloride and 1 ml of Trinder reagent[8] was added. The violet colour produced was measured at 530 nm. It sholud be noted that when the test reagent was added to sodium lauryl sulfate solution, white turbidity appeared. The appearance of turbidity was prevented by the addition of benzalkonium chloride. Each study was done in triplicate and the absorbance was measured against a blank treated similarly.

RESULTS AND DISCUSSION

The hydrolysis of aspirin solution, at 35°C. and at a variety of pH values was investigated. Also the effect of increasing concentrations of SLS, up to 10%, was investigated. The hydrolysis of aspirin was found to proceed at first order rates both in the

presence and absence of SLS. Figures 1-4 are typical plots for the hydrolysis of aspirin solution at pH 1, 2.4, 7 and 9 respectively either alone or in presence of different concentrations of SLS. From these figures one can elucidate that a fall in the hydrolysis rate was attained as the concentration of the surfactant was elevated.

The rate constants for aspirin hydrolysis were calculated by means of a least square regression analysis. The rate constant-pH profile for the hydrolysis of aspirin at 35°C is shown in Fig. 5. An increase in the pH value from 1 to 2.4 is accompanied by a sharp decrease in the rate constant. An increase in the pH value from 2.4 to 6 was found to be accompanied by an increase in the rate constant, while, a plateau region was observed at pH 6 to pH 7 followed by an increase in the rate constant from pH 8 to pH 9. From this figure it could be concluded that the presence of SLS did not alter the optimum pH value for the hydrolysis of aspirin, pH 2.4. This behavior is in general agreement with the findings of Ismail and Simonelli[6,7].

From Figure 5 and Table 1, it would appear that the hydrolysis of aspirin solution was dependent on the concentration of SLS used. An addition of the surface active agent in adequate excess amount was accompanied by a decrease in the rate constant and prolongation of the half-lives.

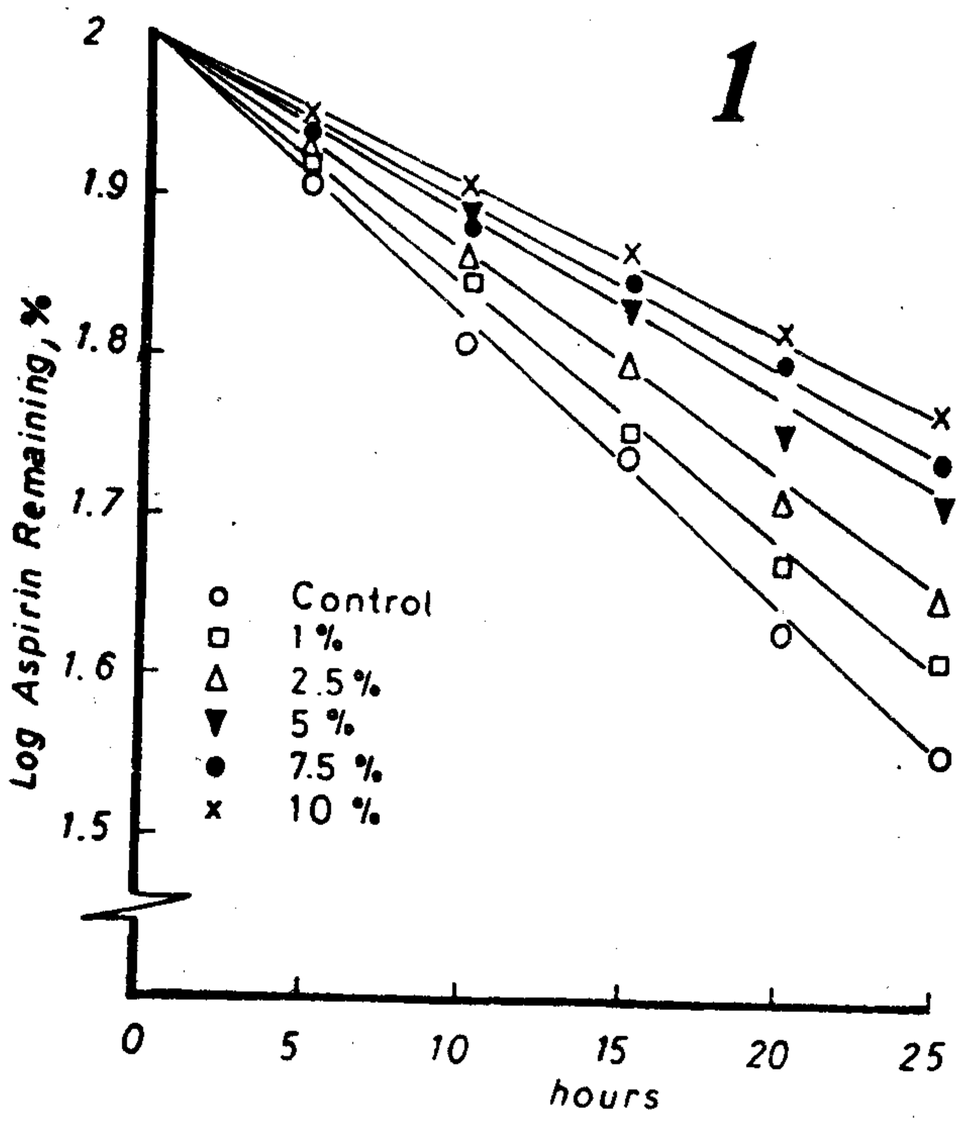
The reduction in the rate of aspirin hydrolysis could be explained on the basis that addition of SLS will reduce the actual amount of aspirin present in the true aqueous phase which is ready to be hydrolyzed. The molecules located inside the micelles are les accessible to hydrolytic attack and the rate of reaction will fall. It is an acceptible suggestion that the rate of reaction is controlled, partly, by the charge on the micelles. Thus, in acidic medium the hydronium ions will be attracted to the anionic micelles of SLS and contrarily in the alkaline medium the hydroxyl ions will be repelled.

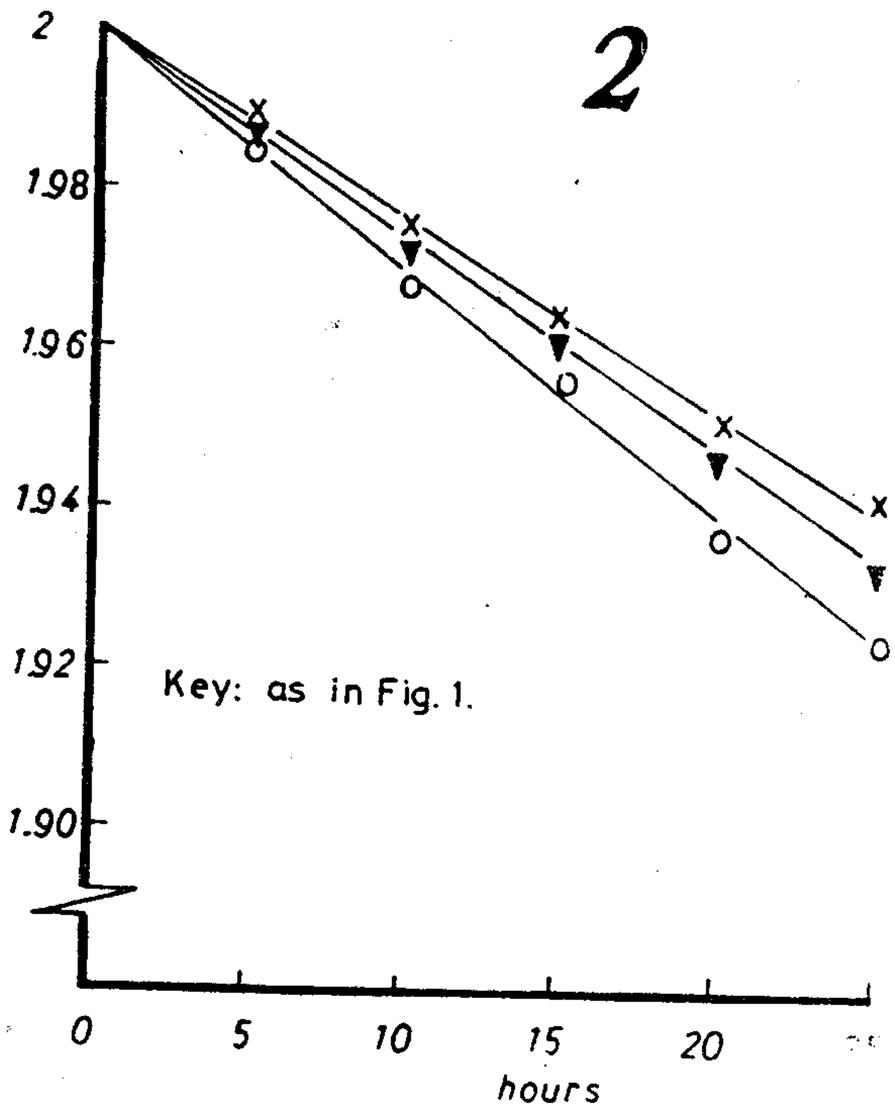
The phenomena of attraction and repulsion of the specific acid-base catalysis is considered as one of the most important factors that may affect the rate of hydrolysis of the ester. From Figure 5 it is clearly observed that in acidic region from pH 1 to pH 2.4, the presence of SLS protects aspirin against hydrolysis. This unexpected data could be explained on the basis that the solute distributes itself between the micellar and the aqueous phases and since it is preferntially soluble in the micellar phase an increase in the surfactant concentration will increase the amount of the solute transferred into this phase relative to that in the true aqueous phase. In alkaline medium, besides the reduction in the amount of ester available in the true solution it is possible that the charged atmosphere around the micelles may act as a partial barrier to the penetration of the hydroxyl ions to come in contact with aspirin molecules burried within the micellar core.

Kinetics of Aspirin Hydrolysis in Aqueous Solutions of Surfactants III: Sodium Lauryl Sulfate.

Table 1: Effect of pH Variation and SLS Concentration on the Half-Lives of Aspirin at 35°C.

pH	$t_{\frac{1}{2}}$, hr, in presence of the following SIS Concentrations % w/v.					
	0	1	2.5	5	7.5	10
1	16.99	18.73	21.52	25.57	27.72	30.80
1.4	35.53	36.47	40.53	42.77	44.71	46.20
1.8	75.32	76.15	77.86	79.66	80.58	82.50
2.4	103.43	105.00	110.00	111.77	115.50	117.46
3	60.26	63.00	67.28	73.65	77.00	81.53
4	29.12	32.23	36.47	43.31	47.79	51.33
5	23.57	27.18	31.50	37.06	43.31	45.89
6	22.28	26.15	29.87	35.90	39.60	43.31
7	20.74	24.32	27.28	32.23	38.07	41.25
8	20.87	24.57	27.18	32.53	38.50	41.75
9	15.93	18.18	20.87	23:81	27.72	30.13





FIGURES 1-4 : First-Order Plots for the Hydrolysis of Aspirin in Absence and Presence of Sodium Lauryl Sulfate at 35° C.
1; pH 1 , 2; pH 2.4 , 3; pH 7 and 4; pH 9.

Kinetics of Aspirin Hydrolysis in Aqueous Solutions of Surfactants : Sodium Lauryl Sulfate.

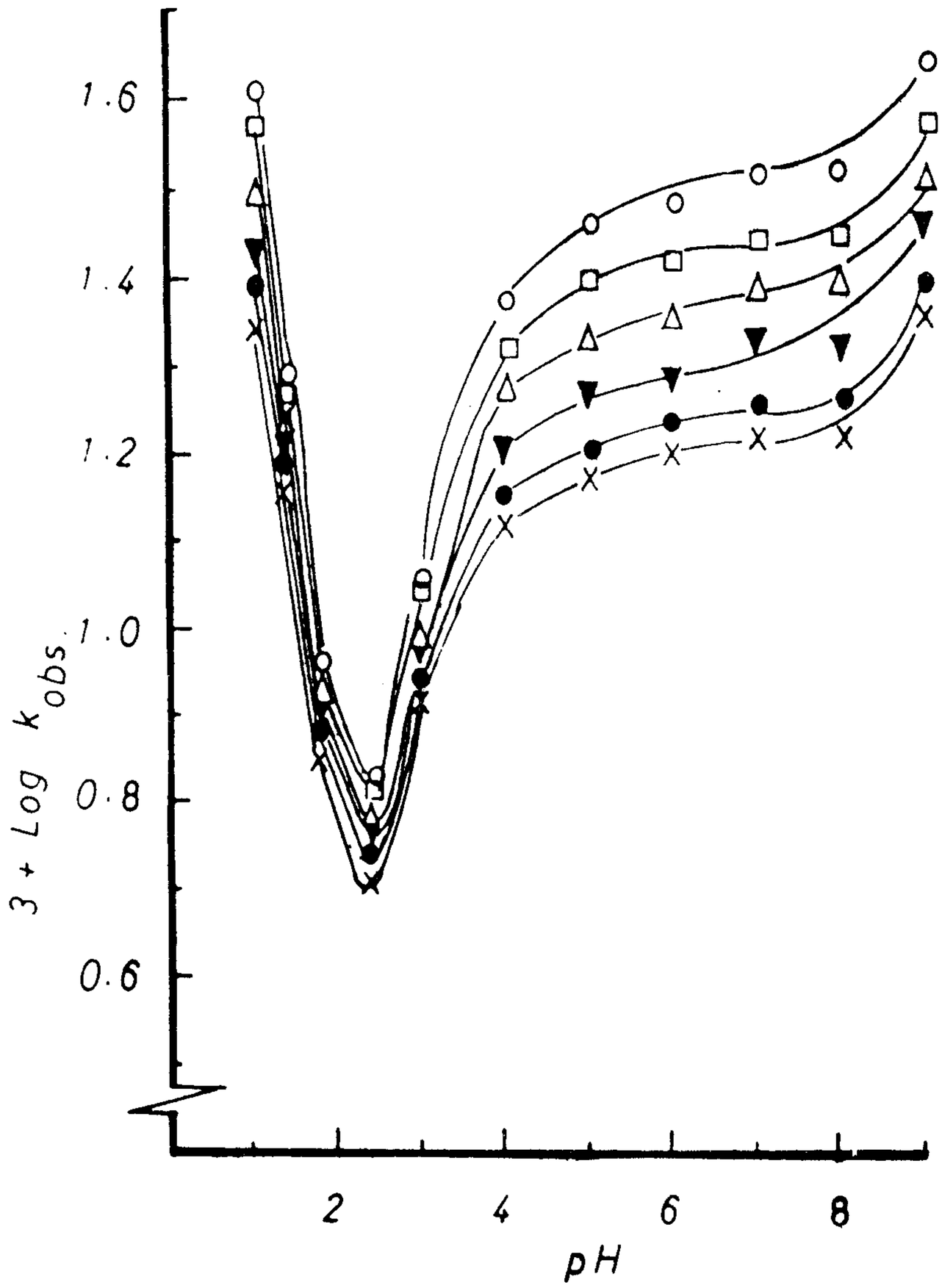


FIGURE 5. pH Profile for the Hydrolysis of Aspirin at 35°C in Absence and Presence of Sodium Lauryl Sulfate.

Key: as in Figure 1.

REFERENCES

1) A.G. Mitchell, J. Pharm. Pharmac., 16, 43 (1964)

2) Ibid., 15, 761 (1963).

3) Ibid., 14, 172 (1962).

4) S.A. Khalil, M.A. Moustafa, V.F. Naggar and M.M. Motawi, Canad. J. Pharm. Sci., 7, 109 (1972).

5) M.A. Kassem, A.A. Kassem and A.E.M. El-Nimr, Die Pharmazie, 26, 359 (1971).

6) S. Ismail and A.P. Simonelli, Bull. Pharm. Sci., Ass. Univ, 9, 119 (1986).

7) Ibid, Bull. Fac. Pharm. Cairo Univ., 24, 107 (1985).

8) D. Trinder, Biochem. J., 57, 301 (1954).

9) Documenta Geigy,"Scientific Tables", Geigy, Basel, 7th Ed., p- 280.

معدلات تميؤ الاسبرين فى محاليل المنشطات السطحية

٣-كبريتات لاوريل الصوديـــــوم

سيد اسماعيلمحمد ـ أنتـــونى بسيمونيللى×

قســـــم الصيدلانيات ـ كلية الصيدلة ـ جامعة أسيوط ـمصـــر

× قسم الصيدلانيات ـ كلية الصيدلة ـ جامعة كونيكتيكـــــــت

الولايات المتحدة الامريكية

تم فى هذا البحث دراسة معدلات تميؤ الاسبرين عند أرقام هيدروجينية مختلفة تراوحت بين ق يد ١ الى ق يد ٩ وفى وجود تركيزات متزايدة من كبريتات لاوريـــل الصوديوم عند درجة حرارة ٣٥°م . وقد دلت النتائج على أن كبريتات لاوريـــــل الصوديوم تسببت فى حماية الاسبرين من التميؤ وأن درجة الحماية تعتمد على تركيز كبريتات لاوريل الصوديوم . وقد فسرت النتائج على أساس أنه كلما ازداد تركيـــز المنشط السطحى فان الاسبرين يقوم بتوزيع نفسه بين الشباك والوسط المائـــــى المحيط . وأن كمية الاسبرين التى توجد داخل الشباك تزداد كلما زاد تركـــــيز المنشط السطحى وعلى النقيض فان كمية الاسبرين الموجودة فى المحلول المائـــــى المحيط بالشباك والقابلة للتميؤ السريع فانها تنخفض . كما أوضحت الدراســة أن وجود المنشط السطحى لم يغير من قيمة الاس الهيدروجينى الامثل لثبات محلـــــول الاسبرين وهى ق يد ٢ر٤ .

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