*Bull. Pharm. Sci., Assiut University*
*Vol, 9 Part 1, pp 11 - 24*

# ADSORPTION OF ROTOXAMINE TARTRATE BY AVICEL pH 101

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## ABSTRACT

*The adsorption of rotoxamine tartrate (RT) by avicel pH 101 was studied at a variety of pH values and in the presence of different concentrations of sodium lauryl sulfate (SLS), sodium cholate (SC), PVP 44000 and different electrolytic species.*

*The results obtained were well described by the Langmuir equation. The limiting adsorptive capacity and the affinity constant were calculated. The data revealed that as the pH value was increased the limiting adsorptive capacity (a value) decreased.The results also revealed that as the concentration of SLS or SC was increased the affinity of the drug to be adsorbed was decreased. The adsorption of RT was found to be dependent on the type of the electrolyte used. It was found that the degree of adsorption decreased as the valence of the basic radicle of the elyctrolyte increased. PVP was found to have a suppression effect on the amount of RT adsorbed by avicel. Interpretation of the results obtained is also offered.*

## INTRODUCTION

Microcrystalline cellulose has been extensively used as a tablet excipient in tablet formulation prepared by either direct compression[1] or wet granulation[2] technique. In the wet granulation process, the active ingredient is often dissolved in the granulating liquid and, therefore, the possibility of the active ingredient to be adsorbed onto avicel surface is increased. The adsorptive prop-

erties of cellulose cannot be disputed. Adsorption studies of some drugs, to the insoluble cellulose derivatives, have been conducted[3,4].

*In vitro* studies show that certain materials, used as pharmaceutical adjuncts, can adsorb significant amounts of various phenothiazines[5]. The adsorption effects on drug absorption had been noted[6,7]. The effect of adsorbents on the rate and extent of promazine absorption from the gastrointestinal tract has been investigated[8,9]. The authors concluded that the forces, through which the adsorption is mediated, are important to the effects obtained *in vivo* and so, it could be concluded that it may be possible to predict the *in vivo* effects from the experimental *in vitro* study.

Up till now the research articles dealing with the adsorption of RT on avicel pH 101 are rare. In this work the adsorption of RT on avicel pH 101 has been investigated at a variety of pH values and in the presence of some pharmaceutical additives. The aim of this study was to investigate the adsorption behavior between rotoxamine tartrate (RT) and a microcrystalline cellulose (avicel pH 101).

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## EXPERIMENTAL

### Materials:

Rotoxamine tartrate[a], microcrystalline cellulose (Avicel) of grade pH 101[b], sodium lauryl sulfate[c], PVP 44000[c], sodium cholate[d], sodium chloride[e], potassium chloride[f], magnesium chloride[c], calcium chloride[e], cobalt chloride[g], disodium hydrogen phosphate[e], citric acid monohydrate[d] and hydrochloric acid[h].

### Adsorption Study:

An accurately weighed 200 mg of avicel pH 101 having particle size of 63 -90 μm was placed into a 50 ml glass stoppered tube. A 20 ml-sample of rotoxamine tartrate solution. being tested, was introduced in the stoppered tube. The tubes were rotated at 50 r.p.m. in a thermostatically controlled water-bath adjusted at 25°C for four hours ( the time required for equilibration). The initial concentrations of the drug used, in each experiment, were 10, 12, 14, 16 and 18 mg per 100 ml. After the equilibrium time has been attained, 1 ml sample was withdrawn from each tube by means of a 1 ml pipette fitted in its end with a polyethylene tube containing a piece of cotton. The sample was analyzed for its drug content spectrophotometrically[i] at 224 nm after suitable dilution with distilled water. Each experiment was carried out twice and the average reading was used for calculating the equilibrium concentration, $C_e$ . The absorbance of each sample was measured against a blank similarly treated so as to compensate any absorbance of the trace substances released into the suspension medium by the microcrystalline cellulose.

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a. Mcneil pharmaceutical, Spring House, PA., U.S.A.
b. FMC Co. Philadelphia, PA., U.S.A.
c. British Drug House, Poole, U.K.
d. Merck, Darmstadt, Germany.
e. El Nasr Pharm. Co., Egypt.
f. Fluka AG, Switzerland.
g. The general Chemical and Pharmacrutical Co. LTD, U.K.
h. Prolabo, France.
i. Shimadzu double beam spectrophotometer (Japan).

Attempts were carried out to investigate the effect of pH value, electrolytes, sodium lauryl sulfate, sodium cholate and PVP 44000 on the adsorption of rotoxamine tartrate onto avicel surface. The amount of the drug adsorbed onto the avicel surface was calculated by the difference between the suspension supernatant concentration and the initial one. It should be noted that all the experimental studies were carried out in distilled water except for the effect of pH value where the Clark and Lubs buffer (pH 1.2) was prepared while McIlvaine's buffer was used for the other tested pH values.

## RESULTS AND DISCUSSION

The adsorption isotherms of rotoxamine tartrate by avicel pH 101 were well described with the following Langmuir equation[10]:

$$\frac{C_e}{M} = \frac{1}{ab} + \frac{1}{a} C_e$$

where M is the amount of the drug adsorbed in milligrams per gram of microcrystalline cellulose, $C_e$ is the concentration of the drug remaining in the suspension supernatant in mg / 100 ml after equilibrium adsorption is attained, a and b are constants. The constant a is termed the limiting adsorptive capacity. It is the maximum amount of adsorbate, in milligrams, that can be adsorbed by one gram of adsorbent. The constant ab is usually termed the affinity constant, and it may be used as a measure for the relative affinity of the sorbate to sorbent[11-13]. This affinity constant is often used when there is a lack of data points at extremely low drug concentration. Therefore, when $C_e/M$ is plotted versus $C_e$ a straight line will be obtained with a slope of 1/a and intercept of 1/ab. The values for the limiting adsorptive capacity (a) as well as the affinity constant (ab) were calculated and tabulated in Table 1.

*Adsorption of Rotoxamine Tartrate by Avicel pH 101.*

The pH-adsorption behavior of rotoxamine tartrate by avicel pH 101 is graphically illustrated in Fig. 1. This figure shows that as the pH value was increased from 1.2 to 5 the adsorptive capacity was decreased. This is most likely due to the ionization of the carboxylate groups on the microcrystalline cellulose surface with an increase in the pH value of suspension. Also as the pH value increased, a free base is subsequently formed. It is assumed that the free base possesses negative centers on both nitrogen and oxygen atoms which results therefore in a decrease in the extent of the drug adsorbed on to avicel surface.

The effect of different concentrations of sodium lauryl sulfate on the adsorption of rotoxamine tartrate is graphically presented in Fig. 2. Both the figure and the table revealed that as the concentration of SLS was increased, the adsorptive capacity was increased. The same behavior was attained in the presence of different concentrations of sodium cholate as shown from Fig. 3. This observation could be explained on the basis that as the surfactant concentration was increased, the surface tension was decreased and accordingly a part of the drug molecules, as a free, may be probably adsorbed onto surface of the microcrystalline cellulose. As a part of the free base was adsorbed, a new free one was transformed. This will continue until the equilibrium between the free base adsorbed and that in solution has been attained.

Figure 4 and table 1 revealed that the adsorption of RT by avicel was markedly repressed in the presence of PVP 44000. The results showed that as the concentration of PVP was increased, the amount of the drug adsorbed was markedly decreased. This behavior may probably be explained on the assumption that some PVP molecules are adsorbed onto the surface of avicel resulting

in a decrease in the number of the vacant sites, on avicel surface, available for the adsorption process.

The effect of added electrolytes on the adsorption of rotoxamine tartrate by avicel is illustrated in figure 5. The results indicate that the extent of drug adsorption is affected by the cationic species used. The divalent cations seem to cause a major decrease in the amount of the drug adsorbed to avicel, as compared with monovalent cations. This may be due to the fact that divalent cations neutralize twice as much as monovalent cations do. This results in a decrease in the number of the negative sites, on the adsorbent surface available for the adsorption process. Also, the divalent cations have a great tendency to be adsorbed on the surface of avicel than the monovalent cations. Therefore less molecules would be adsorbed due to increased competition for the negative surface of the microcrystalline cellulose.

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**Table 1 : The Langmuir Constants for the Adsorption of Rotoxamine Tartrate on Avicel pH 101.**

| Condition of the adsorption medium | (a) (mg/g) | (b) (100ml/mg ) | (ab) |
|---|---|---|---|
| Control | 1.779 | 0.123 | 0.218 |
| pH 1.2 | 3.703 | 0.195 | 0.727 |
| pH 2.2 | 2.439 | 0.363 | 0.887 |
| pH 3.0 | 2.070 | 0.260 | 0.843 |
| pH 4.0 | 1.757 | 0.584 | 1.027 |
| pH 5.0 | 1.587 | 0.584 | 0.928 |
| 0.1 % W/V SLS | 1.639 | 0.166 | 0.272 |
| 0.2 % W/V SLS | 1.736 | 0.190 | 0.330 |
| 0.3 % W/V SLS | 2.050 | 0.156 | 0.323 |
| 0.4 % W/V SLS | 2.984 | 0.057 | 0.229 |
| 0.025 % W/V SC | 1.285 | 0.376 | 0.483 |
| 0.050 % W/V SC | 1.545 | 0.226 | 0.349 |
| 0.100 % W/V SC | 2.487 | 0.089 | 0.222 |
| 0.025 % W/V PVP 44000 | 1.312 | 0.205 | 0.268 |
| 0.050 % W/V PVP 44000 | 1.013 | 0.314 | 0.318 |
| 0.100 % W/V PVP 44000 | 0.797 | 0.734 | 0.586 |
| 0.200 % W/V PVP 44000 | 0.709 | 1.810 | 1.288 |
| 0.2 M Cobalt Chloride | 0.635 | 0.190 | 0.121 |
| 0.2 M Calcium Chloride | 0.699 | 0.177 | 0.123 |
| 0.2 M Magnesium Chloride | 0.748 | 0.172 | 0.129 |
| 0.2 M Potassium Chloride | 0.691 | 0.374 | 0.259 |
| 0.2 M Sodium Chloride | 1.159 | 0.088 | 0.102 |

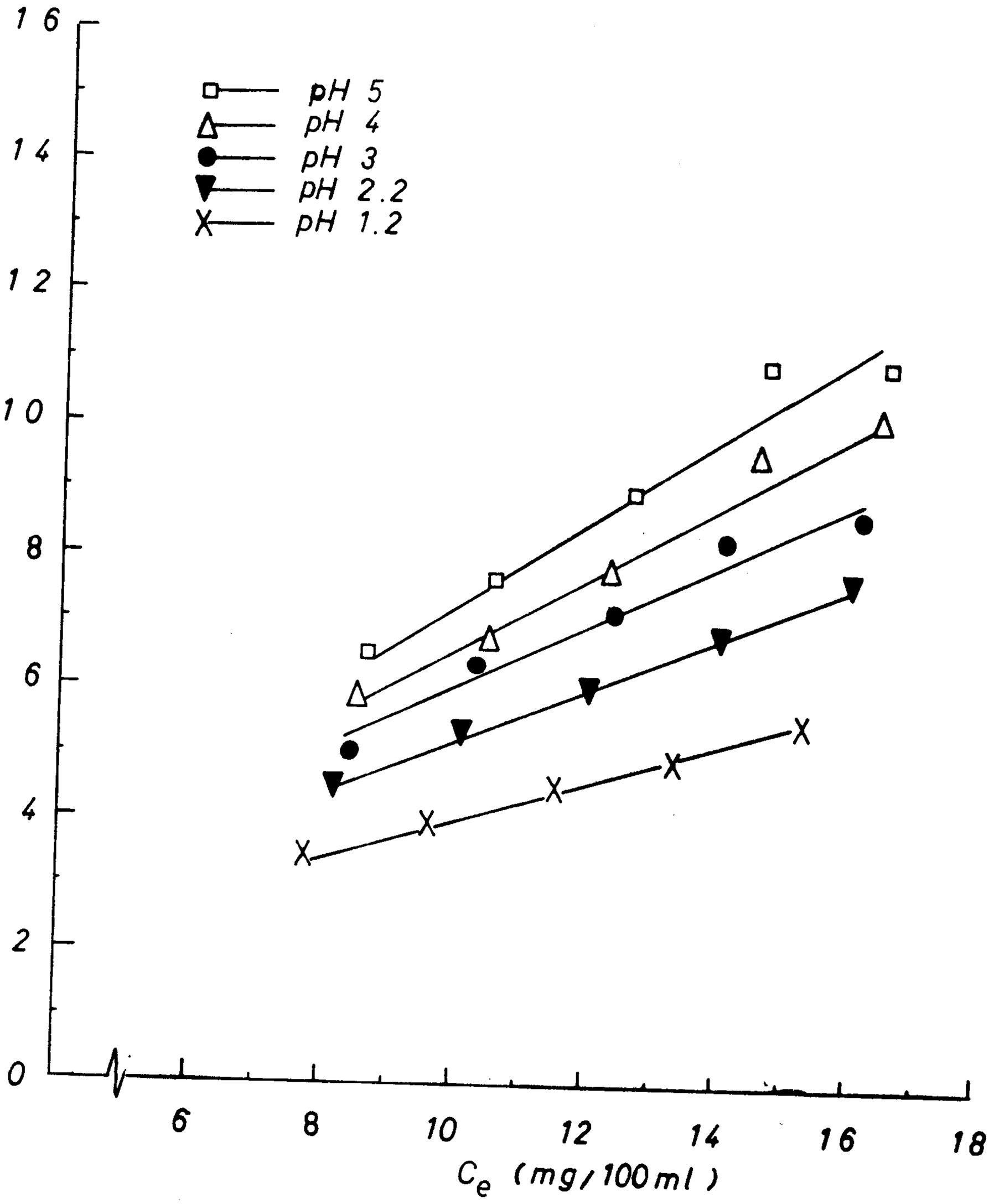


FIGURE 1

THE LANGMUIR'S PLOT FOR THE ADSORPTION OF (RT) BY AVICEL pH 101 AT A VARIETY OF pH VALUES.

*Adsorption of Rotoxamine Tartrate by Avicel pH 101.*

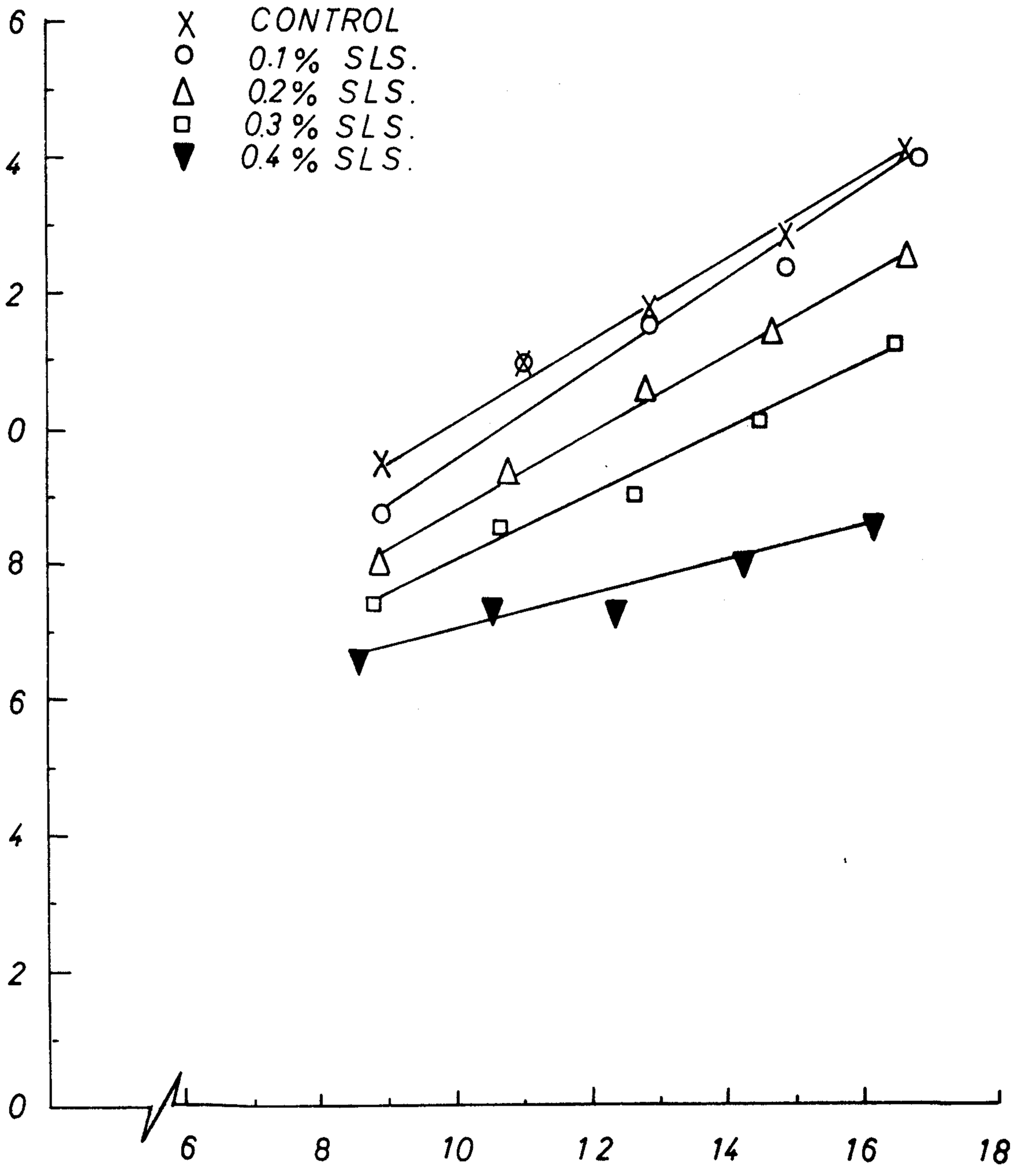


FIGURE 2

THE LANGMUIR'S PLOT FOR THE ADSORPTION OF (RT) BY AVICEL pH 101 AND IN PRESENCE OF DIFFERENT CONCENTRATIONS OF SLS.

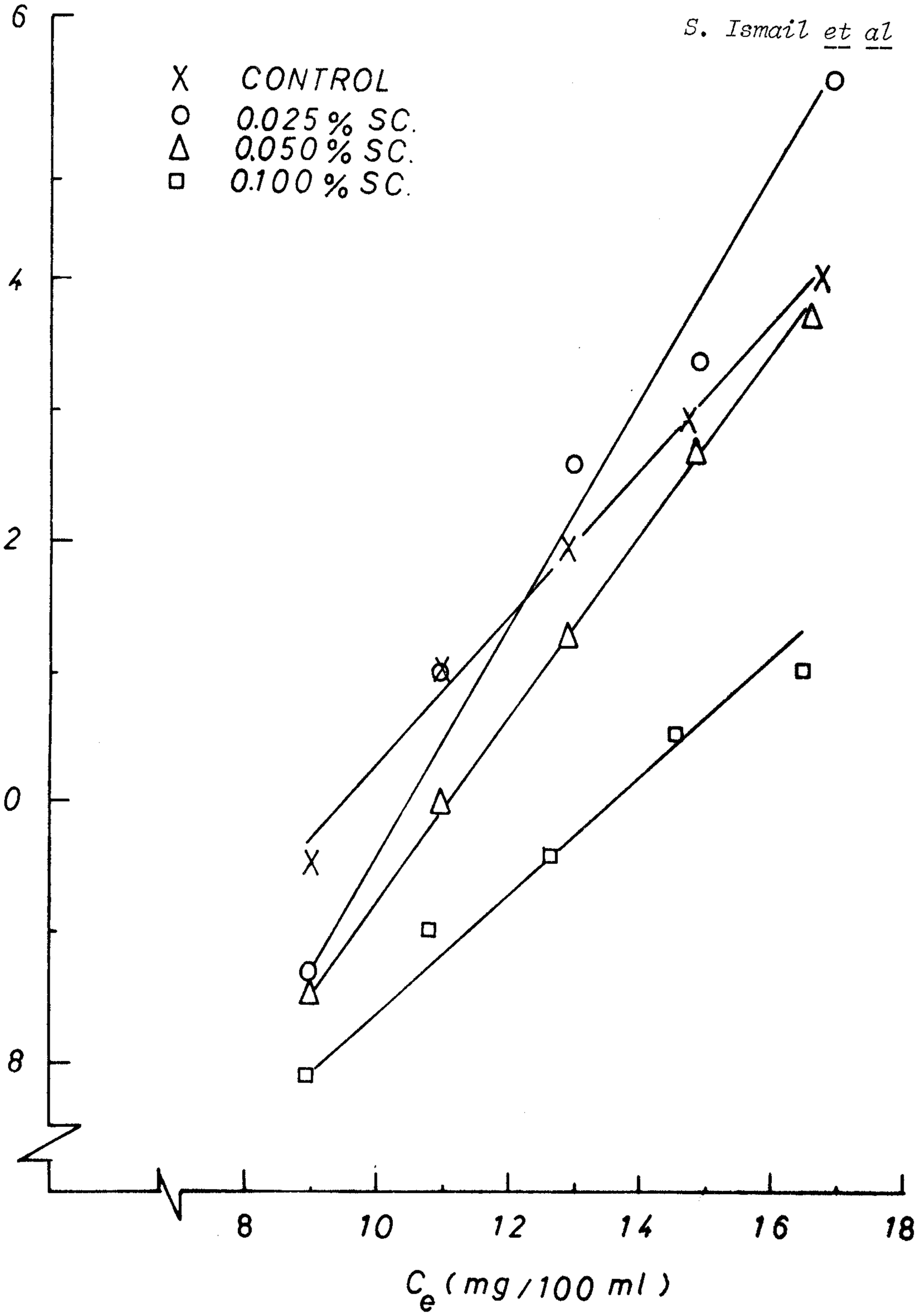


FIGURE 3

THE LANGMUIR'S PLOT FOR THE ADSORPTION OF (RT) BY AVICEL pH 101 AND IN PRESENCE OF DIFFERENT CONCENTRATIONS OF SC.

*Adsorption of Rotoxamine Tartrate by Avicel pH 101 .*

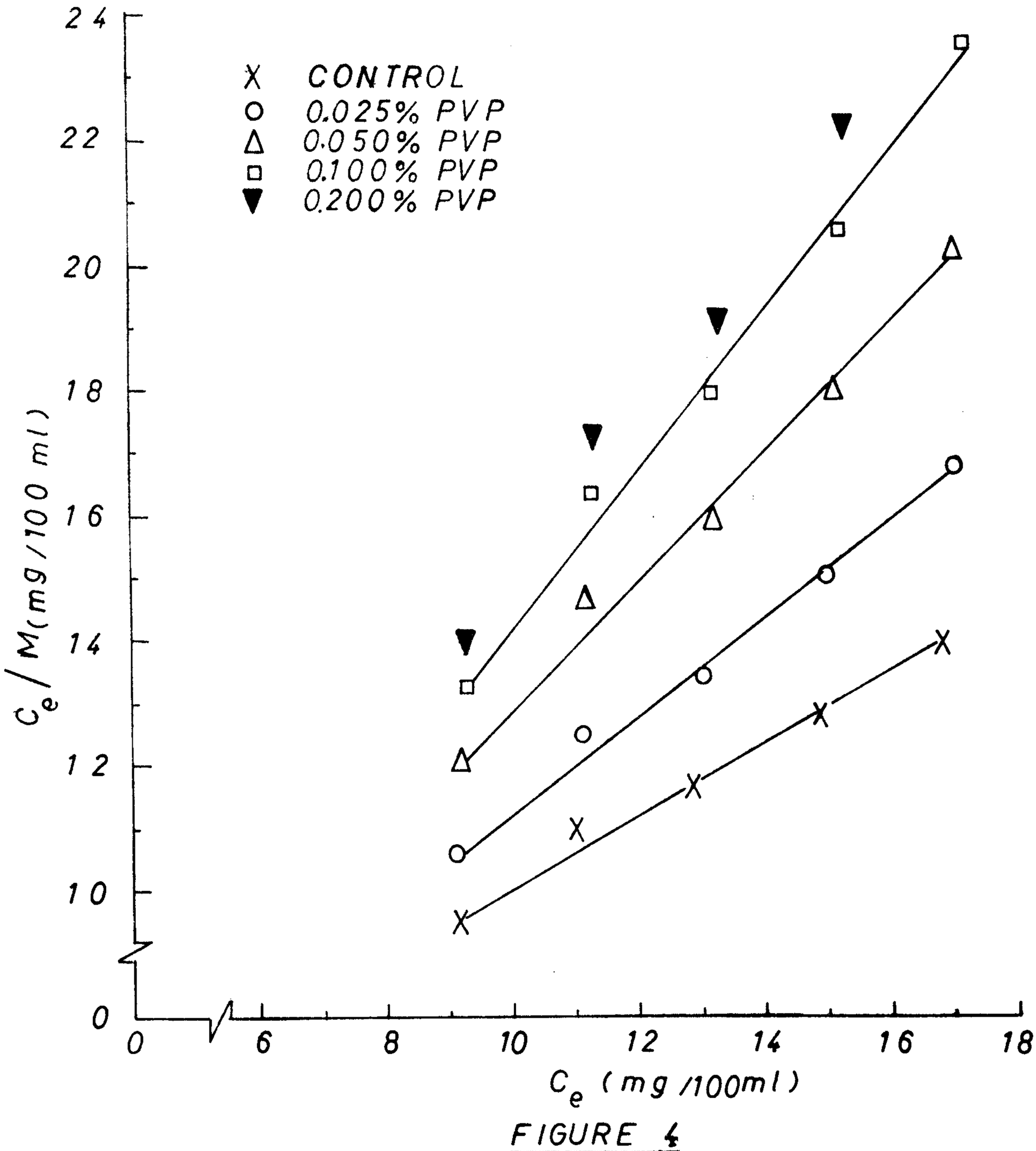


FIGURE 4

THE LANGMUIR'S PLOT FOR THE ADSORPTION OF (RT) BY AVICEL pH 101 AND IN PRESENCE OF DIFFERENT CONCENTRATIONS OF PVP 44000.

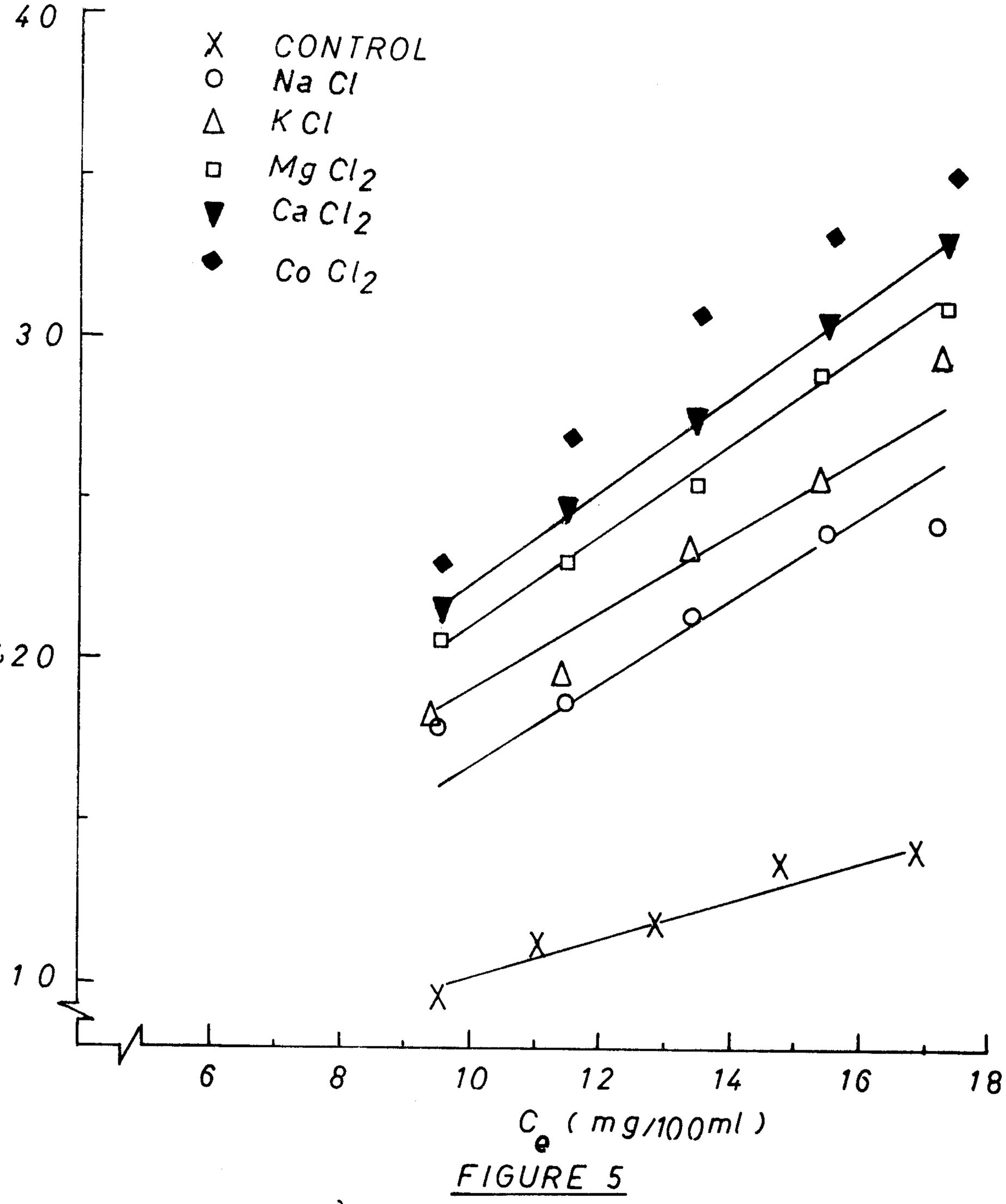


FIGURE 5

THE LANGMUIR'S PLOT FOR THE ADSORPTION OF (RT) BY AVICEL pH 101 AND IN PRESENCE OF DIFFERENT ELECTROLYTES.

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# ادمصاص طرطرات الروتوكسامين بواسطة الافيسيل

سيد اسماعيل محمد - سهير مصطفى الشنوانى

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تم فى هذا البحث دراسة ادمصاص طرطرات الروتوكسامين على الافيسيل وذلك عند ارقام هيدروجينية مختلفة وكذلك فى وجود تركيزات مختلفة من كبريتات الصوديوم ، كولات الصوديوم ، عديد فينيل البيروليدون وكذلك فى منحلات كهربائية هى كلوريد الصوديوم ، كلوريد البوتاسيوم ، كلوريد الكالسيوم ، كلوريد المغنسيوم وكلوريد الكوبالت .

ولقد اثبتت التجارب ان درجة الادمصاص قد انخفضت كلما زاد الرقم الهيدروجينى .

ولقد لوحظ انه كلما زاد تركيز المنشط السطحى المستخدم كلما قلت عملية الادمصاص ويرجع ذلك الى زيادة التوتر السطحى . اما فى حالة المنحلات الكهربائية فلقد لوحظ ان كمية العقار المدمصة تقل كلما زادت الشحنة الموجبة على الايونات كما لوحظ ان الايونات الثنائية تقلل من ادمصاص العقار عن الايونات الاحادية ، وعند استخدام عديد فينيل البيروليدون لوحظ ان درجة الادمصاص قد قلت بزيادة التركيز المستخدمة - ويعزى ذلك الى ادمصاص عديد فينيل البيروليدون على سطح الافيسيل مما يقلل عدد النقاط السلبية على سطح الافيسيل والتى تتم عليها عملية الادمصاص .

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*received in 8/1/1986 & accepted in 10/3/1986*