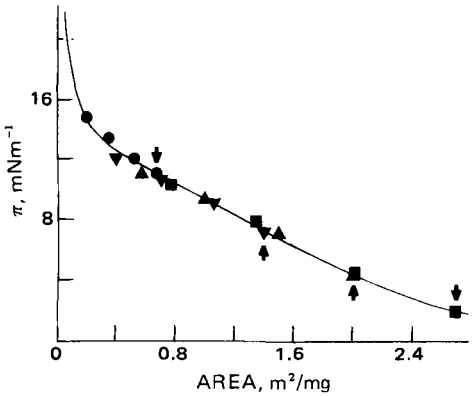

Figure 4—*Comparison of π–A results obtained from adsorbed films (see text for details) with those from a spread monolayer. This solid line is the π–A curve for the compressed monolayer (6). Symbols correspond to those in Fig. 3. Arrows indicate the data points that were fit to the π–A curve of the spread monolayer and from which surface area values of the other points were calculated.*

In Fig. 4, all of the data are combined and compared with the π–*A* curve for a spread monolayer. The correspondence obtained suggests that the structure of the adsorbed monolayers is identical or very similar to that of a spread monolayer, in contrast to what was observed with other polymers.

Concentration of a monolayer by addition of more of the copolymer (in solution) to the surface leads to surface pressure values equivalent to those obtained by compression of a monolayer (6). Therefore, the added copolymer molecules are incorporated to yield a system identical to that obtained by compression of an extremely dilute surface film. Spreading in the presence of a monolayer is similar to the process that occurs during adsorption in that the molecules arriving at the surface in both situations must take their place against the resistance of an existing surface pressure (5). Thus, the ability of the copolymer to spread in the presence of a monolayer to reach a quasiequilibrium state is consistent with the evidence obtained in the present study for the structural equivalence of spread and adsorbed monolayers of the copolymer.

Attainment of the final shape and orientation of an adsorbing polymer molecule is a two-step process. In the first step, the polymer molecule touches the interface and "sticks." At this point, the conformation of the molecule is the same, or nearly the same, as in the bulk phase. In the second step, if it occurs, the molecule rearranges itself to minimize contact of hydrophobic groups with the aqueous liquid while permitting immersion of polar groups. This rearrangement usually involves a change from a coiled conformation to one that is more extended.

Adsorption of the open conformation typical of completely spread molecules requires breaking intramolecular bonds, which represents an energy barrier to molecular rearrangement. In addition, the surface pressure of neighboring molecules in the interface must be overcome since the change to the extended conformation requires additional area at the interface. Another possible hindrance to spreading is intermolecular interaction between adsorbing molecules or between an adsorbing molecule and one that has achieved the open conformation. This interaction would tend to fix the adsorbing molecule in place, making it difficult to reorient in the interface. If these barriers are operative, molecular reorientation can be extremely slow, and the majority of adsorbed molecules will then retain a conformation similar to that in bulk.

Polyvinylpyrrolidone copolymer molecules are highly flexible, and the monolayers are fluid (6). These findings argue against significant intra- or intermolecular association and help to explain why adsorbed films are fully spread. Proteins, however, show significant interactions (13). This fact may account for the differences between spread and adsorbed monolayers of proteins.

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NOTES

Polarographic Analysis of Cephalexin

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Abstract □ Cephalexin was found to be polarographically reducible after hydrolysis in an acidic medium, producing two polarographic waves. Both waves were diffusion controlled. The concentration–diffusion plot method was used for the analysis of cephalexin in capsules.

Keyphrases □ Cephalexin—polarographic analysis in dosage forms □ Polarography—analysis of cephalexin in dosage forms □ Antibacterials—cephalexin, polarographic analysis in dosage forms

Cephalexin[1] is a semisynthetic analog of cephalosporin C in which the α-aminoadipic acid of cephalosporin C is replaced by phenylglycine and the ester-linked acetic acid is condensed to a simple methyl group.

Electrochemical analysis of cephalosporins, specifically, cephalosporin C and derivatives (1, 2) and cefamandole

[1] Recalcine Inc.

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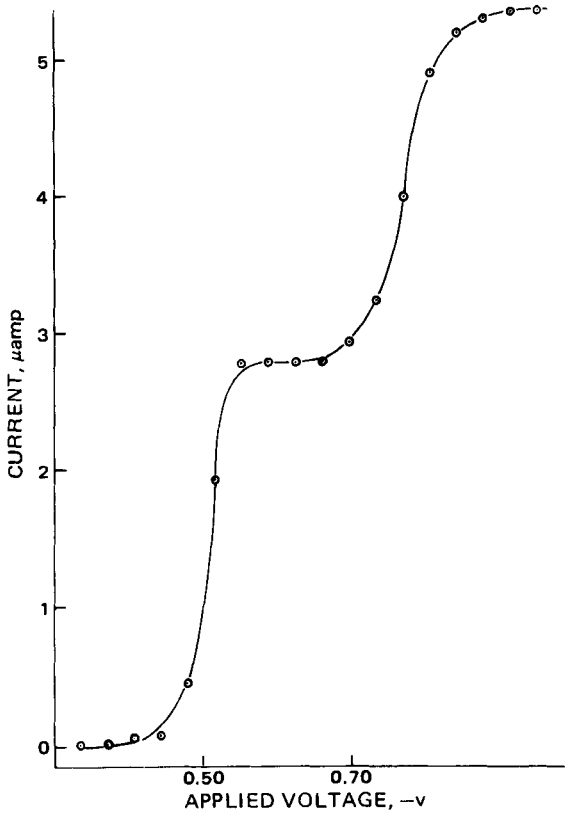

Figure 1—*Polarogram for 6.15 × 10⁻³ M cephalexin in 5.0 N HCl.*

nafate (3), was reported. This paper reports the polarographic behavior of cephalexin and its application to pharmaceutical analysis.

EXPERIMENTAL

Polarograms were recorded using a three-electrode polarograph[2] and a three-compartment polarographic cell. A saturated calomel reference electrode and a 0.5-cm² platinum foil counterelectrode were used. The dropping mercury electrode had an $m^{2/3}\,t^{1/6}$ value of 2.67 at −0.70 v *versus* the saturated calomel electrode in nitrogen-saturated 5.0 *N* HCl.

The current range was 5–7 μamp for the full scale of the recorder, and the potential scan rate was 2 mv/sec. The samples were scanned between −0.30 and −0.90 v *versus* the saturated calomel electrode.

Standards were prepared by accurately weighing 200–300 mg of standard cephalexin[3] and dissolving and diluting in 5.0 *N* HCl to 100 ml.

[2] Tacussel assembly, potentiostat type PRT 20-2, Pilote type Servovit, and recorder type EPL-2

[3] I.S.F. SpA. Rome and Recalcine Inc.

Table I—Results of Six Polarographic Analyses of Cephalexin in Capsules [a]

Analysis	i_d, μamp	Cephalexin per Capsule, mg
1	3.17	262.0
2	3.14	259.0
3	3.18	263.0
4	3.21	266.0
5	3.16	261.0
6	3.16	261.0
Average		262.0
SD		±2.4%

[a] Pentocetin capsules, Recalcine; analyzed by Recalcine Certificate of Analysis No. 10324. This sample contained 263 mg of cephalexin/capsule.

These solutions were heated to 80 ± 0.5° in a constant-temperature bath for 15 min. In a separate study, hydrolysis was complete after 12 min of treatment under the described conditions.

Each sample[1] (commercially available capsules) was dissolved completely in 5.0 *N* HCl, and the same procedure for the standard was followed.

Standard solution and samples were purged with oxygen-free nitrogen for 10 min and polarographed at 25 ± 1°.

The half-wave potentials, $E_{1/2}$, and the diffusion current, i_d, were determined graphically using the maximum of the recorder trace.

RESULTS AND DISCUSSION

Cephalexin does not exhibit polarographic waves without previous treatment. After hydrolysis in 5.0 *N* HCl at 80° for 15 min, two polarographic waves were obtained. The half-wave potentials of waves I and II were −0.50 and −0.78 v *versus* the saturated calomel electrode, respectively. A typical polarogram of cephalexin is shown in Fig. 1.

A plot of diffusion current against the square root of the mercury column height (corrected for back pressure) is a straight line. This result indicated that both reduction waves were diffusion controlled.

Wave I was selected for analytical purposes. Its polarographic current showed a linear relation for levels of cephalexin between 1×10^{-2} and 1×10^{-5} *M* in 5.0 *N* HCl (correlation coefficient for 10 values = 0.99).

The concentration–diffusion current plot method was used for the analysis of cephalexin capsules. The equation of this line is:

$$\text{concentration (mg/100 ml)} = -56.57 + 100.38\, i_d \text{ (μamp)} \qquad \text{(Eq. 1)}$$

Wave I was well developed, and the precision of the proposed method is indicated by Table I.

This method can be recommended for acidic degradation studies of cephalexin and analogous drugs.

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