Penetration of Polymer Monolayers

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Abstract □ Monolayers of polyvinylpyrrolidone copolymers interact more strongly with dissolved benzoic acid than with *p*-hydroxybenzoic acid. In bulk solutions of polyvinylpyrrolidone, the latter is more highly bound. This difference is ascribed to the highly oriented structure which polymers assume at interfaces.

Keyphrases □ Polyvinylpyrrolidone copolymers—monolayer interaction with benzoic acid and *p*-hydroxybenzoic acid, orientation of polymer at interface, effect on penetration □ Monolayers, polyvinylpyrrolidone copolymers—interaction with benzoic acid and *p*-hydroxybenzoic acid, orientation of polymer at interface, effect on penetration □ Penetrability—interaction of polyvinylpyrrolidone copolymer monolayers with benzoic acid and *p*-hydroxybenzoic acid, orientation of polymer at interface

Many important properties of polymers are dependent upon their surface activity. One approach which has proven useful in the elucidation of surface characteristics of polymers is to study them as monolayers at the air–water interface. Monolayer experiments have been used to explain the antifoaming action of silicones (1, 2). Other studies have dealt with polymers used as adhesives (3), emulsion stabilizers (4), and lubricants (5). A great deal of effort has been devoted to the study of monomolecular films of proteins in an effort to gain insight into the structure and properties of biological membranes (see, for example, *Reference 6*).

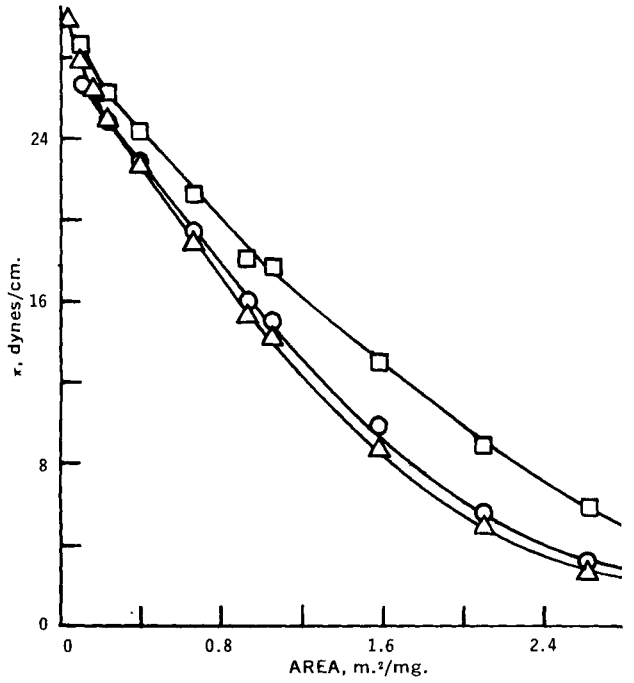

Figure 1—π–A *curves for Copolymer 335. Key:* △, *water subphase;* ○, *subphase containing* p*-hydroxybenzoic acid, 1 g./l.; and* □, *subphase containing benzoic acid, 0.5 g./l.*

One great strength of the monolayer technique is that certain polymer properties may be investigated at the molecular level. It is thus possible to observe interactions between the polymer at the surface and dissolved molecules or ions which are capable of penetrating the surface layer. Studies of this type are useful in evaluating the effects of additives on polymer properties.

Interactions between drugs and polymer monolayers used as membrane models may help identify the mode of action of drugs *in vivo*. Several drugs have been shown to modify membrane transport properties which are presumably controlled by enzymes (7). Investigations dealing with interactions between polymer monolayers and dissolved molecules include recent work on adsorption of heparin by cationic polymers (8) and studies of the penetration of gliadin-containing monolayers by quaternary ammonium compounds (9). Monolayers of half-esters of poly(methyl vinyl ether–maleic anhydride) were shown to interact with dissolved plasticizers; differences in the specificity of interaction aided in formulating a proposed surface structure for two of these polymers (10, 11).

The results reported in this article deal with interactions between graft copolymers of polyvinylpyrrolidone and vinyl acetate and two "small" molecules, benzoic acid and *p*-hydroxybenzoic acid.

EXPERIMENTAL

The procedure used in the purification of the polyvinylpyrrolidone copolymers was described previously (12). Copolymer 335 contained 29.2% w/w polyvinylpyrrolidone; Copolymer 735 contained 61.2% w/w polyvinylpyrrolidone. The residual monomer content of both materials was negligible. Water was deionized and distilled from an all-glass still. Organic liquids were of reagent grade and were found to be free of surface-active impurities (13). Other materials were of reagent grade and were not purified further.

The copolymers were spread from an isopropanol–benzene solution on a water subphase using a micrometer syringe (Agla). When the benzoic acid derivatives were included in an experiment, they were dissolved in water and added to the subphase before spreading. Surface pressure was determined by the Wilhelmy plate method. A thermostat (Lauda K-2) was used to maintain subphase temperature at 25 ± 0.1°. The average rate of compression of the monolayers was about 0.1 m.²/mg./min. Minor changes in the compression rate did not affect the results. If the concentration of the copolymer at the surface was increased by spreading additional material, the resultant surface pressure agreed quite well with that obtained by compressing the film to the same concentration.

RESULTS AND DISCUSSION

The results are conveniently represented by plotting surface pressure (π) as a function of surface area available to the polymer (Figs. 1 and 2). Each data point represents the average obtained from at least two independent experiments. In these experiments, subphase concentration of benzoic acid and of *p*-hydroxybenzoic acid corresponded to about 12% of the solubilities of the respective compounds. Penetration into the polymer monolayer caused expansion

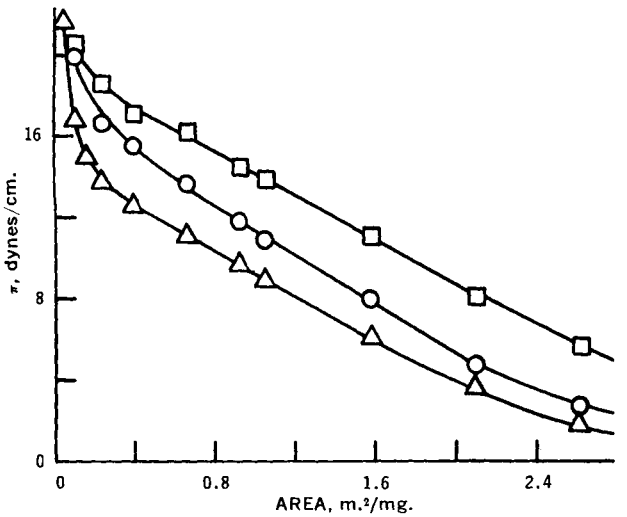

Figure 2—π–A *curves for Copolymer 735. Key:* △, *water subphase;* ○, *subphase containing* p-*hydroxybenzoic acid, 1 g./l.; and* □, *subphase containing benzoic acid, 0.5 g./l.*

of the area occupied by each polymer unit and resulted in a surface pressure above that exhibited by the monolayer containing polymer only.

Figure 1 shows that Copolymer 335 is penetrated by benzoic acid but that the effect of *p*-hydroxybenzoic acid is quite small. Copolymer 735 interacts with both substances (Fig. 2); once again, benzoic acid is more strongly adsorbed than is *p*-hydroxybenzoic acid. Although both of these substances are bound by polyvinylpyrrolidone in bulk solution, *p*-hydroxybenzoic acid is more strongly bound than benzoic acid (14, 15); the opposite is true in the monolayer experiments. It is possible that this difference is due to the more highly organized and spatially oriented structure which polymers assume at an interface (11). Benzoic acid, with a single hydrophobic group located at one end of the molecule, can assume an orientation in which the polar group is immersed in the subphase and the benzene ring extends above it in contact with nonpolar polymer groups. *p*-Hydroxybenzoic acid is not as easily accommodated at the interface, because this molecule has a polar group at each end.

Based on the results reported here, one may conclude that orientation in a polymer monolayer may be a determining factor in monolayer penetration by dissolved molecules. Furthermore, it is dangerous to extrapolate data obtained in bulk solution studies to conditions at interfaces or membranes.

REFERENCES

(1) H. W. Fox, P. W. Taylor, and W. A. Zisman, *Ind. Eng. Chem.*, **39**, 1401(1947).

(2) N. L. Jarvis, *J. Phys. Chem.*, **70**, 3027(1966).

(3) J. Glazer, *J. Polym. Sci.*, **13**, 355(1954).

(4) L. E. Nielson, R. Wall, and G. Adams, *J. Colloid Sci.*, **13**, 441(1958).

(5) H. E. Ries, Jr., and D. C. Walker, *ibid.*, **16**, 361(1961).

(6) F. MacRitchie and N. F. Owens, *J. Colloid Interface Sci.*, **29**, 66(1969).

(7) W. D. Stein, "The Movement of Molecules Across Cell Membranes," Academic, New York, N. Y., 1967, pp. 281–295.

(8) L. Vroman and A. L. Adams, *J. Colloid Interface Sci.*, **31**, 188(1969).

(9) D. W. Blois and J. Swarbrick, paper presented before the Basic Pharmaceutics Section, APhA Academy of Pharmaceutical Sciences, San Francisco meeting, Mar. 1971.

(10) J. L. Zatz, N. D. Weiner, and M. Gibaldi, *J. Pharm. Sci.*, **58**, 1493(1969).

(11) J. L. Zatz, N. D. Weiner, and M. Gibaldi, *J. Colloid Interface Sci.*, **33**, 1(1970).

(12) J. L. Zatz and B. Knowles, *J. Pharm. Sci.*, **60**, 1731(1971).

(13) J. L. Zatz, *ibid.*, **59**, 117(1970).

(14) T. Higuchi and R. Kuramoto, *J. Amer. Pharm. Ass., Sci. Ed.*, **43**, 398(1954).

(15) P. Molyneux and H. P. Frank, *J. Amer. Chem. Soc.*, **83**, 3169(1961).

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New Compounds: Amides Derived from [(10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)thio]acetic Acid

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Abstract □ Synthesis of sulfide amides from [(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)thio]acetic acid is described. Preliminary pharmacological results are reported.

Keyphrases □ Amides—synthesized from [(10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)thio]acetic acid, pharmacological screening □ [(10,11-Dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-yl)thio]acetic acid—used as a starting material for synthesis of sulfide amides, products tested for pharmacological activity □ Antihistamines, potential—synthesis of sulfide amides, pharmacological screening

Many compounds of diversified chemical structure have been found to possess histamine-antagonizing activity (1–6). In addition to this activity, many possess other pharmacological activities including antispasmodic, sedative, local anesthetic, sympathomimetic, and antiacetylcholine actions (7). Studies have attempted to find a more selective antihistaminic activity, including analogs possessing the sulfide linkage (8).