

# Monomolecular Film Properties of Protective and Enteric Film Formers II: Evaporation Resistance and Interactions with Plasticizers of Poly (Methyl Vinyl Ether/Maleic Anhydride)

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**Abstract** □ Surface pressure-area isotherms of monolayers of the half-esters of poly (methyl vinyl ether/maleic anhydride)(PVM/MA) on aqueous subphases indicate interactions between the polymer and various water-soluble diester plasticizers. Polymer monolayers, either alone or in the presence of plasticizer, have no effect on water evaporation. Certain monolayer properties of the PVM/MA derivatives are related to properties of the polymers in free films.

**Keyphrases** □ Molecular properties—protective enteric film formers □ Poly (methyl vinyl ether/maleic anhydride) effect—evaporation □ Plasticizers, interaction—poly (methyl vinyl ether/maleic anhydride) □ Polymer monolayers—plasticizer penetration □ GLC—analysis

In the previous paper (1), monomolecular films were found to provide a useful model system to study the properties of polymers used as film coatings for solid dosage forms. The present report concerns the interactions of polymer monolayers with various water-soluble plasticizers and the penetration of water vapor through polymer and polymer-plasticizer surface films.

Interactions of an insoluble monolayer with a water-soluble substance is conveniently studied by injecting a solution of the substance beneath the monolayer or by dissolving it in the subphase before spreading the monolayer. If no interaction occurs between the components the soluble compound is easily squeezed out of the surface, and the surface properties are identical to the pure monolayer system. If there is a weak interaction, the penetrant dissolves in the monolayer and there is an increase in surface pressure ( $\pi$ ) at a constant surface area ( $A$ ), but the penetrant is gradually squeezed out upon further compression. Strong interactions yield surface complexes of definite stoichiometry whose  $\pi$ - $A$  characteristics differ from those of either component (2, 3).

Goddard and Schulman (4) related the hemolytic potency of various surface-active agents to their ability to penetrate cholesterol films. Schaubman and Felmeister (5) investigated the penetration of lecithin monolayers by chlorpromazine. Pethica (6) studied the penetration of cholesterol monolayers by sodium decyl sulfate. At a constant surface area, the increase in surface pressure, due to penetration, was a function of penetrant concentration, indicating dissolution in the surface rather than formation of a stoichiometric complex.

There have been few reports on interactions in polymer monolayers. Reis and Walker (7) observed a large increase in the collapse pressure of mixed films of stearic acid and poly (vinyl acetate) as compared to the collapse pressure of either component alone, despite the fact that the polymer apparently had been squeezed

out of the film before collapse. In addition, the mixed film could be expanded and recompressed with little hysteresis, in marked contrast to the behavior of stearic acid alone.

Labbauf (8) described the monomolecular film behavior of mixtures of poly (vinyl acetate) and poly (ethyl acrylate). He demonstrated the existence of an interaction and proposed that a similar approach be applied to investigate polymer-plasticizer interactions. However, no studies of this nature have appeared in the literature to date.

The concept of resistance to evaporation by monolayers was introduced by Langmuir and Schaefer (9) who measured evaporation by determining the increase in mass of a desiccant suspended over the surface. La Mer *et al.* (10–18) modified Langmuir's technique and extended the original work. The resistance of a monolayer to evaporation was taken to be analogous to electrical resistance in that resistances in series are additive. Thus, such factors as the resistance of the air above the surface and the resistance of the desiccant may be nulled by subtracting the total resistance of a clean surface from that of the surface monolayer.

Shukla *et al.* (19) studied water evaporation rates by spreading a monolayer on water in a petri dish and periodically weighing the dish. O'Neill and Goddard (20) used chambers containing a vessel of water covered by a monolayer or other artificial membrane and placed the entire assembly in a desiccator containing towers of anhydrous calcium sulfate. Jarvis *et al.* (21) placed a thermistor just below the water surface and compared the surface temperature of a clean surface to that of a surface covered by various monolayers. Substances which had previously been shown to inhibit evaporation produced a significantly higher surface temperature during evaporation as compared to the surface temperature of a clean surface.

The ability of insoluble monolayers to retard evaporation has been ascribed to the presence of an energy barrier (9–11) so that an equation of the form:

$$r = k \exp(E/RT)$$

may be written, where  $r$  is the specific resistance,  $k$  is a frequency factor, and  $E$  represents an activation energy. A plot of  $\log r$  versus  $1/T$  for a fatty acid monolayer yields a straight line, supporting the energy barrier concept (10). The activation energy has been interpreted as the energy required to form a "hole" in the monolayer large enough for a water molecule to pass through (22).

Protein monolayers apparently offer little resistance to water vapor evaporation. Sebba *et al.* (23, 24)

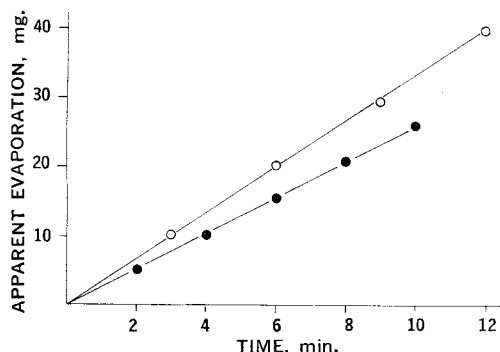


Figure 1—Effect of stearic acid monolayer ( $\pi = 4.5$  dynes/cm.) on the apparent evaporation rate from  $10^{-3}$  M HCl. Key: ●, monolayer; ○, control.

studied these systems with a method in which dry air was passed over a monolayer on a surface balance. Moisture picked up by the air was then collected and weighed. The presence of protein monolayers, regardless of their surface pressure, had no effect on the evaporation rate. More recently, Blank and Musselwhite (25) measured evaporation from protein solutions by dipping a phosphor bronze or glass ring in the solution under investigation, and monitoring its change in mass with time as evaporation was allowed to proceed. The authors conclude that proteins offer an extremely small, but finite, resistance to evaporation under the conditions of their experiment.

#### EXPERIMENTAL

**Materials**—The ethyl and *n*-hexyl half-esters of poly (methyl vinyl ether/maleic anhydride) (PVM/MA) were prepared and purified as previously described (1). The plasticizers employed were Eastman grade, Eastman Organic Chemicals. Isopropyl alcohol and *n*-hexane were reagent grade. All organic liquids were repeatedly passed through a silica gel-alumina column, prior to use, to remove surface-active impurities. Purity was checked by a model 810 gas chromatograph equipped with a column containing 10% synthetic hydrocarbon (Apiezon L) on 60–80 mesh diatomaceous earth (Diatoport W). All organic liquids were found to exhibit a single peak.

Water was deionized by passing through a mixed resin bed of a Bantam demineralizer at the rate of 150–200 ml./min. and then fractionally distilled in an all glass still. All inorganic chemicals were reagent grade. Glassware was cleaned in chromic acid solution and rinsed in hot distilled water prior to use.

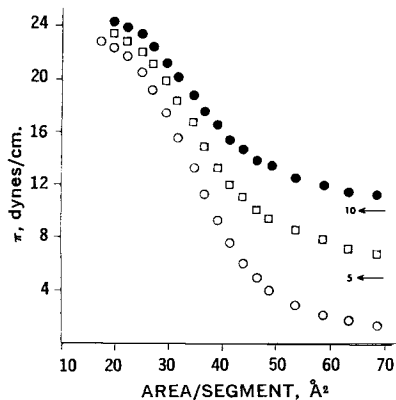


Figure 2—Effect of dibutyl adipate (DBA) on the surface pressure ( $\pi$ )-area isotherm of the ethyl half-ester of PVM/MA. Key: ○, polymer alone; □, polymer + DBA (initial  $\pi = 5$  dynes/cm.); ●, polymer + DBA (initial  $\pi = 10$  dynes/cm.).

**Penetration of Polymer Monolayers by Plasticizers**—The surface balance employed was made of Teflon and has been previously described (26). Sufficient plasticizer was dissolved in  $10^{-3}$  M HCl to bring the surface pressure of the subphase to either 5 or 10 dynes/cm. The half-esters of PVM/MA, dissolved in a mixture of isopropanol and hexane, were spread on the subphase by means of an Agla micrometer syringe. Surface pressure was determined as a function of area using the Wilhelmy plate method (27). All experiments were performed at room temperature ( $24 \pm 0.5^\circ$ ).

**Water Evaporation Studies**—A direct weighing method, similar to that of O'Neill and Goddard (20) was employed. The balance used was a Sartorius analytical balance model 2462 (Brinkmann Instruments, Inc.). Sensitivity of the balance with a load of 142 g. was found to be 0.1 mg. The weighing compartment, which contains the pan, has sliding glass doors which may be sealed, thus insulating the weighing compartment from its surroundings. The weighing compartment was therefore used as the drying chamber. This allowed continuous monitoring of evaporation loss without disturbing the apparatus or the monolayer.

Pyrex crystallizing dishes, 40 mm. high and 80 mm. in diameter, were filled with 100 ml. of subphase. The monolayer, when employed, was spread on the subphase in the dish. The entire dish was placed on the pan of the Sartorius balance. Four 100-ml beakers, containing 60 g. of anhydrous calcium sulfate (Drierite, W. A. Hammond Co.) were placed in the weighing compartment, around the dish. The weighing compartment was then sealed and 15 to 20 min. was allowed to elapse to attain steady-state conditions. The weight of the crystallizing dish and its contents was then recorded as a function of time. Studies on evaporation through a monolayer of stearic acid were conducted as a check on the method. As shown in Fig. 1, there is a significant decrease in evaporation rate when a monolayer of stearic acid is present, in agreement with previously published results (9–11). In studies of evaporation through polymer monolayers, the subphase was either  $10^{-3}$  M HCl or  $10^{-3}$  M HCl containing sufficient dibutyl phthalate to yield solutions with surface pressures of 5 or 10 dynes/cm. Sufficient half-ester to attain the desired surface pressure was then spread on the subphase, and water evaporation was determined as a function of time.

#### RESULTS AND DISCUSSION

**Penetration Studies**—Penetration of a monolayer of the ethyl half-ester of PVM/MA by plasticizers is typified by the results obtained with dibutyl adipate, shown in Fig. 2. Corresponding curves demonstrating penetration of the hexyl half-ester monolayer by this plasticizer are presented in Fig. 3.

To interpret the penetration experiments, it is convenient to think of the polymer monolayer as a surface phase. In the expanded region, the surface phase is dilute since the polymer segments are separated by water molecules (1). In the condensed region, polymer segments are in close contact and the surface phase may be considered, as in Fowkes' interpretation (28), to be con-

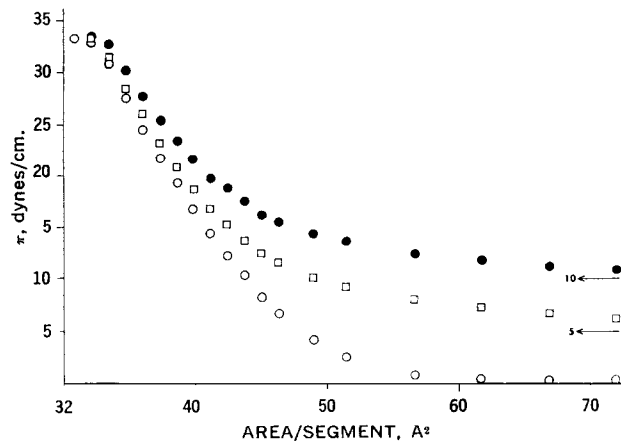


Figure 3—Effect of dibutyl adipate (DBA) on the surface pressure ( $\pi$ )-area isotherm of the hexyl half-ester of PVM/MA. Key: ○, polymer alone; □, polymer + DBA (initial  $\pi = 5$  dynes/cm.); ●, polymer + DBA (initial  $\pi = 10$  dynes/cm.).

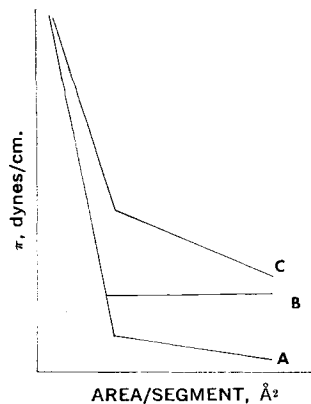


Figure 4—Hypothetical surface pressure-area curves showing penetration of and interaction with an insoluble polymer monolayer by a soluble surface-active agent. Curve A, monolayer alone; Curve B, penetration by surfactant; Curve C, penetration and interaction.

tinuous in polymer segments in which water is dissolved. If there is no interaction between the insoluble polymer monolayer and dissolved plasticizer, both species may simultaneously occupy the surface. In this case, the insoluble monolayer acts merely to decrease the surface area available to plasticizer molecules. To compensate for this reduction in available surface area, some plasticizer molecules leave the surface phase to enter the subphase, and the surface pressure remains unchanged (Curve B in Fig. 4). As the film is compressed, more plasticizer molecules are forced into the bulk (and to the other side of the barrier) and the surface pressure remains constant. When compression causes the surface pressure of the polymer monolayer alone to be greater than that exerted by the plasticizer, all of the plasticizer molecules are forced from the surface and the  $\pi$ -A curve at higher surface pressures will be identical to that obtained in the absence of plasticizer. If an interaction occurs, the plasticizer will dissolve in the surface phase and the surface pressure at a given surface area will be higher than that observed in the absence of an interaction (Curve C in Fig. 4).

Based on these criteria, one may conclude that the diester plasticizer interacts with the half-esters of PVM/MA. This finding is important since it has been shown that penetration depends on an affinity of the polar groups of penetrant and film molecules as well as on an association between the non-polar portions of the molecules (29). Penetration of PVM/MA half-ester monolayers by plasticizers must therefore be the result of a mutual perturbation and not due simply to a "filling of empty space" by available molecules.

The increase in surface pressure of the penetrated monolayer, compared to the polymer monolayer alone, is an indication of the extent of penetration of plasticizer into the surface phase. A large increase in surface pressure may be the result of: (a) a high degree of interaction and/or (b) a high intrinsic affinity for the surface. One method of evaluating the interaction of a polymer with different plasticizers is to eliminate the intrinsic affinity factor by comparing plasticizer-polymer interactions at the same initial surface pressure (though concentrations in the subphase will generally be different). The value of this approach is supported by the curves in Figs. 2 and 3, which show that the degree of penetration is dependent on the initial surface pressure of the plasticizer.

Other diester plasticizers, such as dibutyl succinate and diethyl phthalate, penetrated monolayers of PVM/MA half-esters to very nearly the same extent as dibutyl adipate. The degree of interaction of the polymers with these plasticizers is therefore approximately the same.

It is of interest to note the effect of plasticizer on recompression of a polymer monolayer. If a monolayer, in the presence of dissolved plasticizer, is compressed to collapse, allowed to expand, and then after about five minutes compressed again, the original  $\pi$ -A curve will be duplicated. However, if plasticizer is not present, the second compression curve will exhibit a somewhat lower value at any given apparent area, probably because some of the polymer did not respread when the film was expanded. This diminution of hysteresis is a further indication of interaction.

**Evaporation Studies**—The presence of a polymer monolayer, either alone or in the presence of plasticizer, had no effect on water evaporation (Fig. 5). This observation provides some insight to the structure of the monolayer. Compounds which have been shown to retard evaporation, such as long chain fatty acids and alcohols (11) can assume tightly packed, highly condensed orientations in monolayers (30). It has been postulated that the energy barrier to evapora-

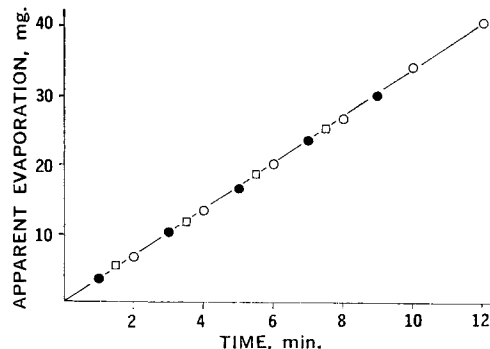


Figure 5—Lack of effect of PVM/MA monolayer on the apparent evaporation rate from  $10^{-3}$  HCl solution containing dibutyl phthalate at an initial surface pressure of 5.5 dynes/cm. Key:  $\circ$ , no monolayer;  $\square$ , monolayer ( $\pi = 23$  dynes/cm.);  $\bullet$ , monolayer ( $\pi = 30$  dynes/cm.).

tion depends on the presence of closely packed nonpolar groups (10). Because the presence of only a small number of spaces or holes causes a profound decrease in evaporation resistance (9) the arrangement of segments of a polymer at the interface would have to allow a very close fit if its monolayer were to inhibit evaporation. This condition apparently was not met in the polymers studied. Close packing may not have been possible because of the presence of bulky side groups.

**Relationships Between Monolayers and Free Films**—Previous workers have shown that the properties of monolayers may often be related to those of bulk systems. Merker and Daubert (31) found such a relation in their study of monoglycerides. Crisp (32) was able to demonstrate a relationship between the spreading properties of various polymers and their bulk characteristics. Fox *et al.* (33) applied the results of their surface studies on polyorganosiloxanes to achieve an understanding of the temperature coefficient of viscosity of the compounds in bulk systems.

The length of the ester side chain of half-esters of PVM/MA has been shown to exert significant influence on the properties of monolayers of these substances (1). The importance of such factors as nonpolar interactions between side chains has also been demonstrated in bulk systems. For example, an increase in ester side chain length causes a decrease in moisture sorption in free films of the half-esters of PVM/MA (34). Since all the derivatives studied have the same polar groups in equal proportion, differences in apparent hydrophobicity may be ascribed to the ester side chain. Furthermore, since monolayer stability is increased by van der Waals' interactions between side chains, hydrophobicity in bulk films should be related, at least qualitatively, to collapse pressure of monolayers of the same derivatives. Figure 6 is a plot of the collapse pressure of the half-esters studied versus their respective apparent moisture sorption (taken from Fig. 8, Reference 34). The plot clearly demonstrates a relationship between bulk and monolayer properties.

Since monolayers of half-esters of PVM/MA exhibit no energy barrier to water evaporation, we may infer that moisture permeation through such films is purely a diffusion controlled process.

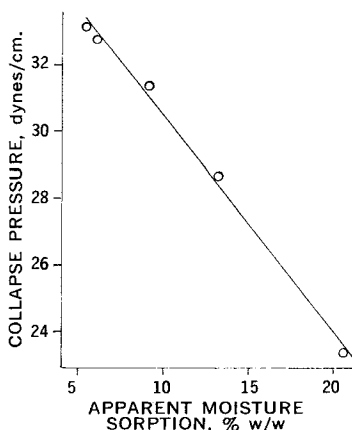


Figure 6—Relationship between collapse pressure of monolayers of various half-esters of PVM/MA and apparent moisture sorption by free films of these esters.

Lachman and Drubulis (35) studied the effect of plasticizers on water vapor permeation through cellulose acetate phthalate films. Increasing the concentration of plasticizer in the film caused first a decrease, and then an increase in water vapor permeation. Banker *et al.* (36) obtained similar results with films of hydroxypropyl cellulose and poly(butyl methacrylate). It was postulated by Lachman and Drubulis that plasticizer fills the interstices of the polymer, reducing permeation. After the interstices are completely filled, further plasticizer has only a dilution effect.

An alternate explanation for this phenomenon is suggested by considering that insoluble polymers with hydrophilic groups may still have considerable affinity for water. Evidence for this is their ability to sorb moisture and to spread as a monolayer on an aqueous substrate. In unplasticized films, water acts both as permeant and plasticizer (37) and its presence in the film provides an additional pathway for permeation. If a plasticizer is included in the free polymer film there is dipole-dipole attraction between the polar portions of both molecules, and induced dipole-induced dipole interactions between the nonpolar portions.

Since polar groups of the polymer are solvated by plasticizer, the role of water as a plasticizer, leading to augmented permeation is diminished. At the same time, plasticizers increase the mobility of polymer groupings and this effect causes an increase in the diffusion coefficient of permeating vapors (38). The net influence of plasticizer on water vapor transmission through polymers depends on the magnitude of the effects cited. At low plasticizer concentrations, although the segmental mobility is increased, the effects of interaction of the plasticizer in decreasing solvation by water is more important and the permeability of the film to water vapor is reduced. As the concentration of plasticizer is increased, the increase in mobility of groupings in the film is the greater effect and, permeation increases.

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