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[x] To whom inquiries should be directed.

Surface Activity of Prostaglandins E_2, $F_{2\alpha}$, A_1, and B_1 in Presence of Insoluble Monomolecular Films

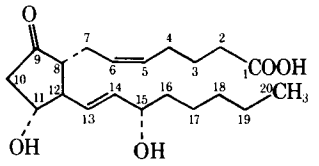
BERNARD SIMS [x] and SHELLY L. HOLDER [*]

Abstract □ Surface activities of four naturally occurring prostaglandins, PGE_2, $PGF_{2\alpha}$, PGA_1, and PGB_1, were investigated by examining the π–A compression isotherms obtained for insoluble monomolecular films of stearic acid spread on subphases containing the prostaglandins. All four compounds were observed to bring about increased instability of stearic acid monolayers, as evidenced by reductions in both transition and collapse surface pressures. Prostaglandin E_2 did not readily penetrate the monolayer but appeared capable of associating with the polar groups of the film, bringing about monolayer instability. PGB_1 exhibited a disruptive effect upon monolayer structure, causing some expansion of the π–A isotherm and increased instability. Prostaglandin $F_{2\alpha}$ penetrated into the stearic acid film, giving rise to increased surface pressure development in the initial regions of the π–A curve, resulting in a significantly expanded isotherm. This same effect, in the case of $PGF_{2\alpha}$, was observed using cholesterol and distearoyl phosphatidic acid monolayers. PGA_1 also appeared to penetrate the stearic acid monolayer, forming a mixed monolayer system and causing considerable rearrangement in monolayer structure as evidenced by an extended plateau region occurring in the π–A plot. The order of surface activities observed for the prostaglandins was $PGA_1 > PGB_1 > PGF_{2\alpha} > PGE_2$. The relative importance of polar functions, hydrophobic interactions, and hydrogen bonding are discussed with respect to the observed effects on monolayer stability. Some biological implications of the data are presented.

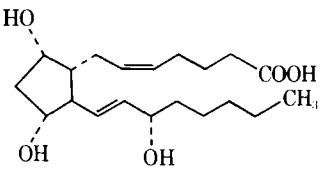
Keyphrases □ Prostaglandins E_2, $F_{2\alpha}$, A_1, and B_1—surface activity in presence of insoluble monomolecular films, π–A isotherms, biological implications □ Surface activity—four prostaglandins in presence of insoluble monomolecular films, π–A isotherms □ Films, insoluble monomolecular—surface activity of prostaglandins □ Monomolecular films, insoluble—surface activity of four prostaglandins

In recent years, great research interest has been directed toward the elucidation of the physical–chemical properties and pharmacological and physiological actions of a new class of hormones, the prostaglandins. Numerous review articles and publications have described their occurrence, synthesis, metabolism, and possible roles in biological processes (1–3). More recently, a journal has appeared devoted exclusively to prostaglandin research.

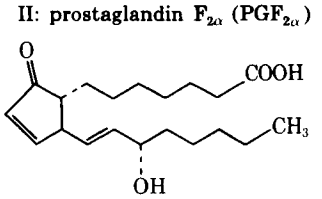
Surprisingly few investigations have concerned their surface activity (4, 5), especially since they have been implicated in various membrane-related functions, *e.g.*, vascular permeability changes (6), vascular resistance (7), intestinal transport of ions (8), binding of calcium to mitochondrial membrane (9), platelet aggregation (10), the inflammatory process (11), and smooth muscle stimulation (12). This study was undertaken to provide insight into the surface activity of four naturally occurring prostaglandins in the presence of simple model membrane systems.



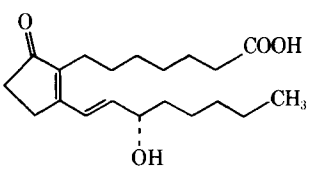
I: prostaglandin E_2 (PGE_2)



II: prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$)



III: prostaglandin A_1 (PGA_1)



IV: prostaglandin B_1 (PGB_1)

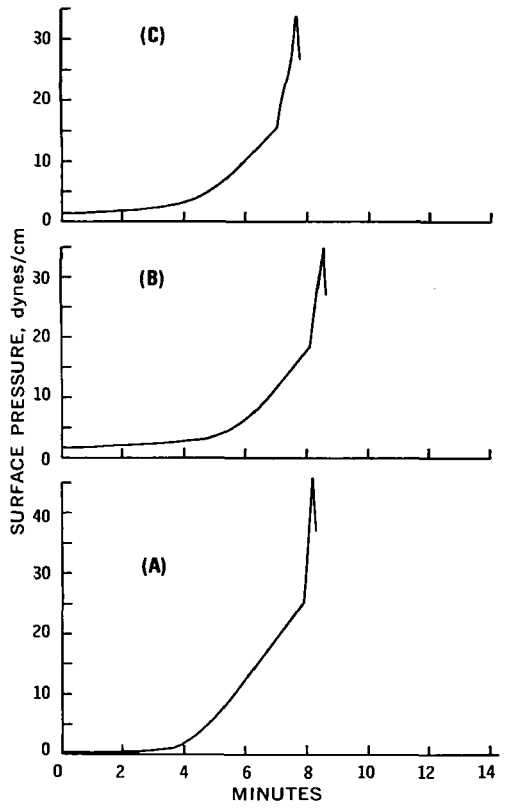


Figure 1—*The π–A compression curves for stearic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0 × 10⁻⁵ M PGE_2, and (C) 0.01 M HCl with 4.0 × 10⁻⁵ M PGE_2. Area per molecule at zero time is 30 Å²; V_0 = 1.2 Å²/molecule/min.*

Stearic acid, distearoyl phosphatidic acid, and a bulky hydrophobic compound with a small polar moiety, cholesterol, were selected for monolayer formation. The prostaglandins investigated were PGE_2 (I), $PGF_{2\alpha}$ (II), PGA_1 (III), and PGB_1 (IV).

The prostaglandins are essentially long-chain unsaturated fatty acids containing a substituted cyclopentane ring system. $PGF_{2\alpha}$ differs from PGE_2 in that the carbonyl group at C_9 is replaced by a hydroxyl function. PGA_1 and PGB_1 are isomeric compounds which differ only in the position of the double bond in the cyclopentanone ring. The *π–A* compression behavior of the three monolayer compounds was examined on pure subphases (without substrate) and compared to the surface behavior exhibited by spreading the same films on subphases containing different concentrations of the prostaglandins. No surface activity was detectable for the prostaglandins alone at the concentrations employed in the subphase.

EXPERIMENTAL

Materials—GC of $PGF_{2\alpha}$[1], PGA_1[1], and PGB_1[1] and TLC–UV analysis of PGE_2[1] indicated a purity of 99.9% for all four compounds. Distearoyl phosphatidic acid[2], stearic acid[2], and cholesterol[2] had a stated purity of 99+%. Spectroscopic grade hexane–chloroform–methanol (20:2:1) was used as the spreading solvent, and water twice distilled with alkaline permanganate from an all-glass apparatus was used to prepare the subphase solutions.

Equipment—The monolayer balance consisted of a Teflon-covered trough having an area of 315 cm² and a width of 10.5 cm. The trough was hollowed out so that water at controlled temperatures could be circulated. The entire unit was enclosed in a large metallic box for protection against dust contamination. The barrier was driven at controlled rates of movement by means of constant revolutions per minute motors equipped with reversible drive and a positive clutch for instant stop.

Surface pressure was measured using the Wilhelmy plate method, utilizing a 5-cm roughened platinum plate. Mass changes were measured with an electromagnetic balance[3] and recorded[4]. The balance was housed in a large metallic box above the trough unit and was situated on an elevating stand to facilitate placement of the plate into the aqueous surface. Since vertical movement of the plate is negligible when this self-balancing unit is used (13, 14), it was possible to minimize error introduced by possible contact angle change at very high surface pressures.

General Procedure—Subphase solutions containing the prostaglandins were prepared in 0.01 *M* HCl at 2.0 × 10⁻⁵ and 4.0 × 10⁻⁵ *M* concentrations. Since it was difficult to assure complete solubility of these compounds above 4.0 × 10⁻⁵ *M*, preparation of more concentrated solutions was not attempted. Preliminary TLC of $PGF_{2\alpha}$, PGE_2, and PGB_1 solutions indicated the compounds to be chemically stable in 0.01 *M* HCl during the experiment. PGA_1 had previously been shown to be stable in acidic media (15). Monolayers of stearic acid, distearoyl phosphatidic acid, and cholesterol were prepared from 1-mg/ml solutions of each component in hexane–chloroform–methanol (20:2:1). These solutions were added to the surface of subphases containing the prostaglandins, utilizing

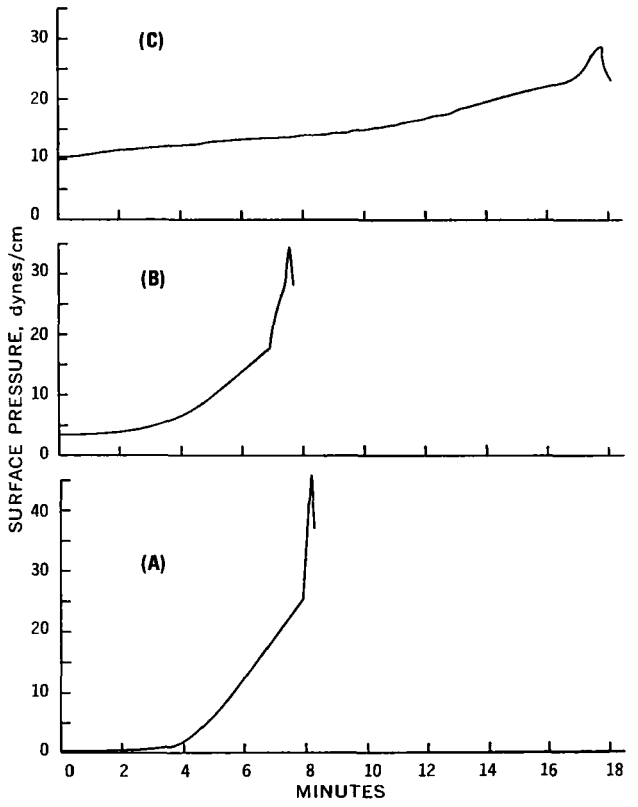


Figure 2—*The π–A compression curves for stearic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0 × 10⁻⁵ M PGF_2, and (C) 0.01 M HCl with 4.0 × 10⁻⁵ M $PGF_{2\alpha}$. Area per molecule at zero time is 30 Å²; V_0 = 1.2 Å²/molecule/min.*

[1] $PGF_{2\alpha}$, PGE_2, PGA_1, and PGB_1 were prepared and made available by The Upjohn Co., Kalamazoo, MI 49001

[2] Applied Science, State College, Pa.

[3] Cahn R.G.

[4] Sargent Welch model SRLG.

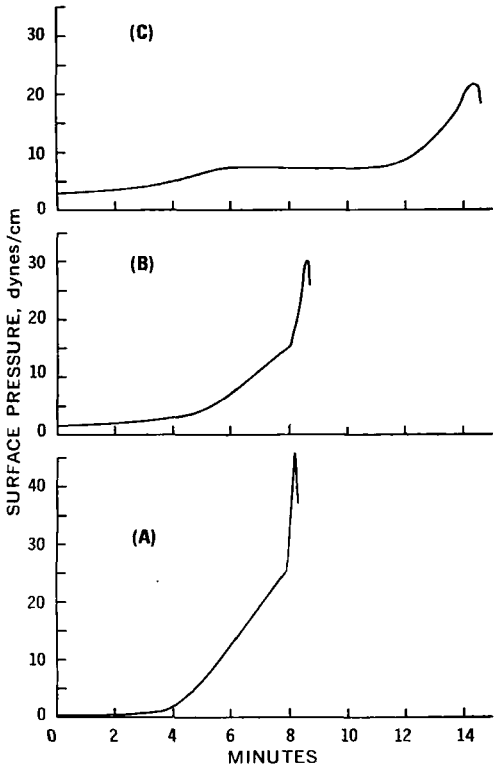


Figure 3—*The π–A compression curves for stearic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0 × 10^{-5} M PGA_1, and (C) 0.01 M HCl with 4.0 × 10^{-5} M PGA_1. Area per molecule at zero time is 30 Å^2; V_0 = 1.2 Å^2/molecule/min.*

a micrometer syringe unit[5] which delivered 20–30 μg of material to the surface at an initially high area per molecule. After allowing 20 min for complete spreading and equilibration, the monolayer was compressed to its collapse point with constant velocity. Each subphase solution was used for only one compression experiment, which lasted for no longer than 20 min. The values reported for surface pressure represent the average of at least three to five independent measurements that differed by no more than ±0.4 dyne/cm. All studies were carried out at 25 ± 0.3°. Spreading of the mixed solvent system alone on 0.01 *M* HCl produced no detectable surface pressure after the 20-min waiting period.

RESULTS AND DISCUSSION

The π–*A* compression plots obtained for stearic acid alone and on 2 × 10^{-5} and 4 × 10^{-5} *M* prostaglandin subphases are presented in Figs. 1–4. Values of specific surface parameters obtained from the isotherms are shown in Table I. The general π–*A* character and surface parameters obtained for stearic acid on 0.01 *M* HCl are in good agreement with results published previously (16). Each plot shown is an actual recorder tracing. Since compression in each case was carried out at constant velocity, the area per molecule at any time point on the graph can be easily calculated.

A great deal of information can be ascertained concerning surface activity of the various prostaglandins by evaluating their effect upon specific monolayer parameters such as $Å_L$, $Å_S$, π_{tr}, and π_c; $Å_L$ is defined to be the limiting area obtained by extrapolation of the liquid-condensed portion of the π–*A* isotherm. This area is generally considered to represent the point at which intermolecular interactions begin to occur among polar head groups of the film-forming molecules (17). It may be used to reflect the presence of molecules that have penetrated the film and that occupy area-determining positions. The term $Å_S$ is the limiting area obtained by extrapolation of the solid-condensed region of the curve and reflects whether molecules that penetrate the film in the liquid or expanded regions are expelled before transition to the solid phase occurs. The transition surface pressure, π_{tr}, and the collapse surface pressure, π_c, may be used to reflect changes that occur in the packing or organization of molecules within the film (17, 18) as well as film stability (19, 20). Transition from a liquid to a solid film represents a point of major reorganization among molecules in the film. Molecules capable of penetration into the surface region could presumably disrupt or alter molecular packing and bring about changes in the monolayer pressure for transition. The collapse surface pressure, π_c, represents the point of maximum monolayer (21) stability, since any effort to compress the film above this pressure results in film collapse. Therefore, a decrease observed in the collapse surface pressure indicates a trend toward increased film instability.

The π–*A* compression behavior observed for stearic acid monolayers on PGE_2 subphases is depicted in Figs. 1B and 1C. The values $Å_L$ and $Å_S$ are comparable to values observed for stearic acid alone on 0.01 *M* HCl (Table I). A pronounced effect of PGE_2 is observed upon the stability of the monolayer, as evidenced by a significant decrease in both the transition surface pressure and the collapse pressure. The transition pressure, at 2 × 10^{-5} *M* PGE_2, is decreased from 25.1 to 18.6 dynes/cm, while π_c is reduced from 46 to 35.2 dynes/cm. This same behavior is accentuated at the higher prostaglandin concentration. These data suggest that PGE_2 molecules do not readily penetrate into the surface region but can apparently associate beneath the surface with film molecules and bring about instability. This may result from dipolar interactions of the prostaglandin molecule with the carboxyl groups of stearic acid and a concomitant disruption in monolayer structure.

Stearic acid monolayers spread on $PGF_{2\alpha}$ subphases (Fig. 2) are noticeably expanded at both concentrations investigated, with $Å_L$ occurring at larger areas per molecule. The expanded character of the π–*A* isotherm suggests that penetration of the monolayer occurs and that prostaglandin molecules assume area-determining positions within the surface. Furthermore, $PGF_{2\alpha}$ alone will not form a stable monolayer when spread on 0.01 *M* HCl and stearic

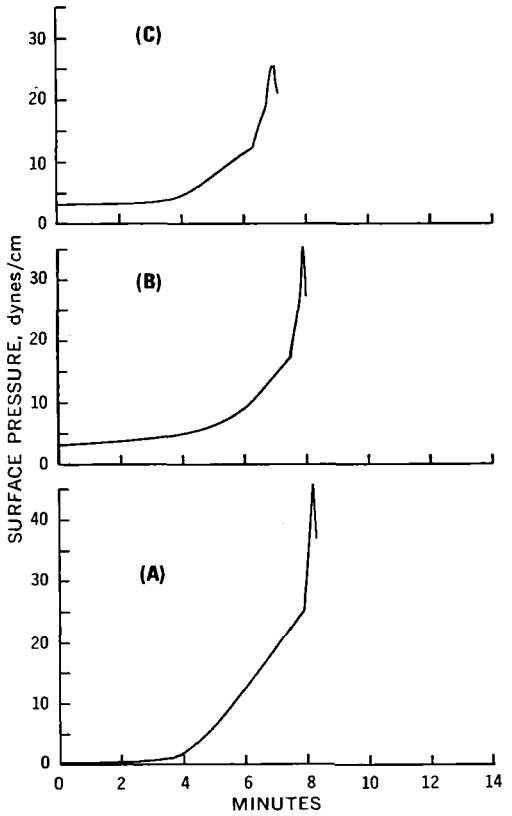


Figure 4—*The π–A compression curves for stearic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0 × 10^{-5} M PGB_1, and (C) 0.01 M HCl with 4.0 × 10^{-5} M PGB_1. Area per molecule at zero time is 30 Å^2; V_0 = 1.2 Å^2/molecule/min.*

[5] Burroughs-Wellcome Agla.

Table I—Values of Specific Surface Parameters Obtained from π–A Isotherms for Stearic Acid Films Spread on Prostaglandin Subphases at 25°

Parameter[a]	0.01 M HCl	PGE_2		$PGF_{2\alpha}$		PGA_1		PGB_1	
		2×10^{-5} M	4×10^{-5} M	2×10^{-5} M	4×10^{-5} M	2×10^{-5} M	4×10^{-5} M	2×10^{-5} M	4×10^{-5} M
A_L, Å²	25.1	23.9	25.2	27.0	—	25.1	—	24.8	26.7
A_S, Å²	20.9	20.8	21.5	21.9	—	21.2	—	21.2	22.7
A_{tr}, Å²	20.5	20.2	21.5	21.8	—	20.3	—	21.0	22.5
A_C, Å²	20.1	19.7	20.7	21.0	8.7	19.6	12.8	20.5	21.7
π_{tr}, dynes/cm	25.1	18.6	15.4	17.5	—	15.2	—	17.1	12.0
π_C, dynes/cm	46.0	35.2	33.9	34.6	29.0	30.0	22.2	35.3	25.7
$\Delta\pi_C$, dynes/cm		10.8	12.1	11.4	17.0	16.0	23.8	10.7	20.3

[a] A_L = limiting area from liquid-condensed region of π–A isotherm; ±0.6 Å². A_S = limiting area from solid-condensed region of π–A isotherm; ±0.6 Å². A_{tr} = area of second-order transition; ±0.6 Å². A_C = area of collapse; ± 0.6 Å². π_{tr} = transition surface pressure, ±0.4 dyne/cm. π_C = collapse surface pressure; ±0.4 dyne/cm. $\Delta\pi_C$ = difference in monolayer collapse surface pressure on pure subphase and subphase containing prostaglandin substrate.

acid alone exhibits only minimal surface pressure in the initial portion of the π–A curve—*viz.*, 30–25 Å²/molecule at 0–4 min (Fig. 2A). The very pronounced surface pressure development in this region on the $PGF_{2\alpha}$ subphase indicates that considerable interaction occurs between the penetrant and film molecules. The presence of hydroxyl groups at both C_9 and C_{11} in $PGF_{2\alpha}$ might account for the increased surface pressure development if intermolecular hydrogen bonding with carboxyl groups of stearic acid occurred. Support for this interaction is obtained by noting in Fig. 1 that PGE_2, which has the C_9 hydroxyl replaced by a keto function (otherwise identical in structure to $PGF_{2\alpha}$), exhibits only minimal surface pressure development in the initial regions of the monolayer π–A curve.

One other activity of this compound on stearic acid monolayers is to decrease the film stability. As can be noted from Table I, at 4×10^{-5} M $PGF_{2\alpha}$, the collapse pressure is reduced from 46 to 29 dynes/cm. Unlike PGE_2, which brings about film instability apparently by association with film molecules, this same effect is achieved with $PGF_{2\alpha}$ by direct penetration of the monolayer and intermolecular association, such that a mixed film system having decreased stability is formed.

Stearic acid monolayers spread on PGA_1 subphases exhibit unusual π–A compression behavior (Fig. 3). At 2×10^{-5} M PGA_1, minimal effect is observed on the value of the limiting areas, $Å_L$ and $Å_S$. This indicates that PGA_1 molecules do not readily penetrate into the monolayer. However, the collapse pressure is substantially reduced from 46 to 30 dynes/cm, so some association apparently can occur among the prostaglandin molecules and stearic acid molecules in the film. In this respect, PGA_1 behaves in similar fashion to PGE_2 in bringing about instability of the monolayer. At the higher PGA_1 concentration (Fig. 3C), a plateau region occurs in the π–A plot at about 7 dynes/cm surface pressure. To account for the plateau, an appreciable number of PGA_1 molecules apparently do penetrate the monolayer at the higher concentration and

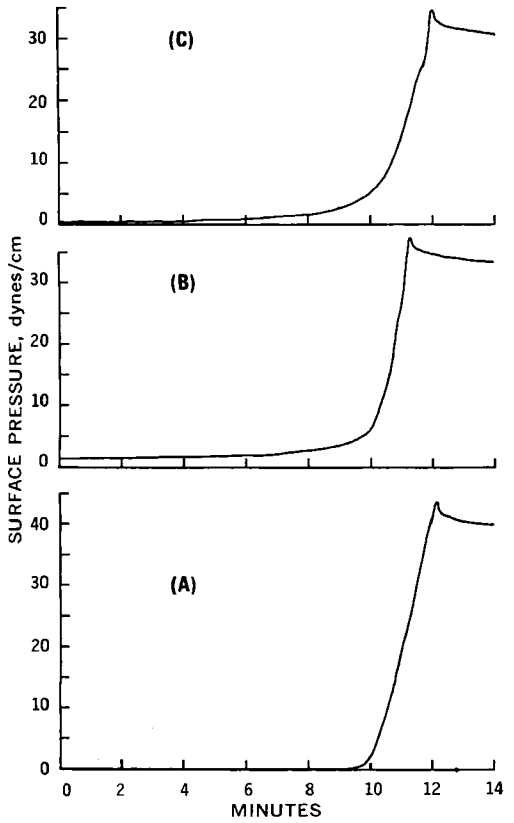


Figure 5—*The* π–A *compression curves for cholesterol monolayers spread on (A) 0.01* M *HCl, (B) 0.01* M *HCl with* 2.0×10^{-5} M PGE_2, *and (C) 0.01* M *HCl with* 4.0×10^{-5} M PGE_2. *Area per molecule at zero time is 75.9* Å²; V_0 = *3.45* Å²/*molecule/min.*

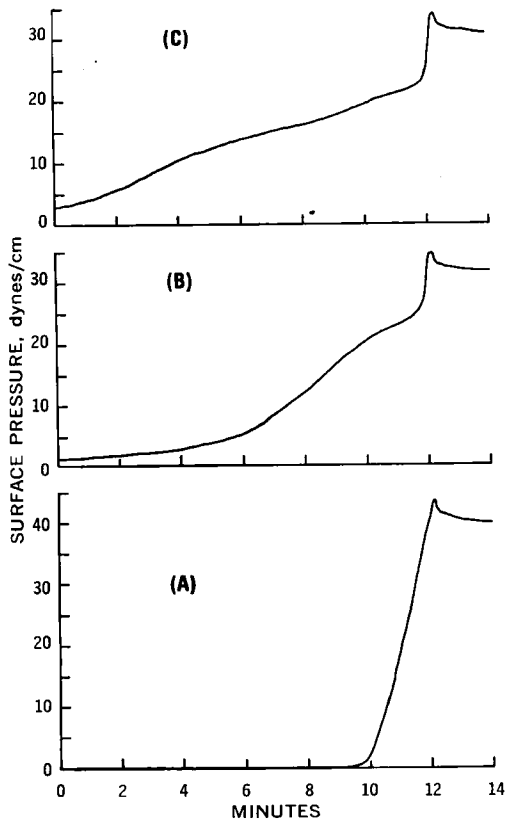


Figure 6—*The* π–A *compression curves for cholesterol monolayers spread on (A) 0.01* M *HCl, (B) 0.01* M *HCl with* 2.0×10^{-5} M $PGF_{2\alpha}$, *and (C) 0.01* M *HCl with* 4.0×10^{-5} M $PGF_{2\alpha}$. *Area per molecule at zero time is 75.9* Å²; V_0 = *3.45* Å²/*molecule/min.*

Table II—Values of Specific Surface Parameters[a] Obtained from π–A Isotherms for Cholesterol Films Spread on PGE_2 and $PGF_{2\alpha}$ Subphases at 25°

	0.01 M HCl	PGE_2		$PGF_{2\alpha}$	
		2×10^{-5} M	4×10^{-5} M	2×10^{-5} M	4×10^{-5} M
A_S, Å²	39.0	39.8	41.2	37.5	36.0
A_C, Å²	34.0	36.9	34.5	34.1	33.5
π_c, dynes/cm	43.8	38.0	34.9	34.4	33.1

[a] Surface parameters have the same definitions given in Table I.

drastically alter monolayer structure. There is considerable rearrangement of molecules within the film. This is evident by the large area over which the plateau extends (23.4–16.5 Å²/molecule) while the film pressure remains constant. The whole π–A curve, in essence, is displaced toward smaller areas per molecule. Following the plateau, monolayer stability is substantially reduced, as seen in the reduction of the collapse surface pressure from 46 to 22.2 dynes/cm. Hence, a dual role can be observed for PGA_1 molecules on the stearic acid system. At low prostaglandin concentrations, they decrease the stability of the monolayer, possibly by association with the polar groups of the film molecules; at higher concentrations, they appear capable of direct penetration into the surface in significant numbers, disrupting monolayer structure and causing significant expansion and rearrangement of film molecules which results in a mixed film system exhibiting decreased stability.

PGB_1, a structural isomer of PGA_1, behaves in a qualitatively similar fashion (Figs. 4B and 4C). At 2×10^{-5} M PGB_1, minimal effect is observed upon the limiting areas, $Å_L$ and $Å_S$. However, the collapse pressure, as in the case of PGA_1, is reduced from 46 to

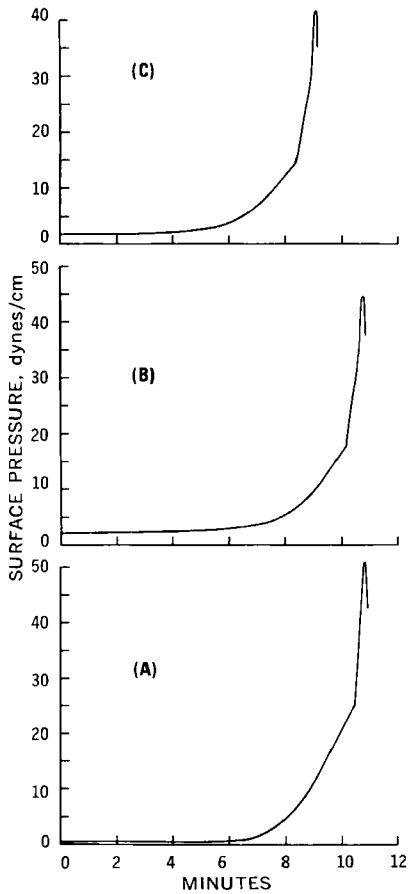


Figure 7—*The π–A compression curves for distearoyl phosphatidic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0×10^{-5} M PGE_2, and (C) 0.01 M HCl with 4.0×10^{-5} M PGE_2. Area per molecule at zero time is 75.9 Å²; V_0 = 3.45 Å²/molecule/min.*

Table III—Value of Specific Surface Parameters[a] Obtained from π–A Isotherms for Distearoyl Phosphatidic Acid Films Spread on PGE_2 and $PGF_{2\alpha}$ Subphases at 25°

	0.01 M HCl	PGE_2		$PGF_{2\alpha}$	
		2×10^{-5} M	4×10^{-5} M	2×10^{-5} M	4×10^{-5} M
A_L, Å²	49.1	49.1	55.6	55.6	—
A_S, Å²	41.0	40.6	46.2	37.7	40.2
A_{tr}, Å²	40.0	40.9	47.0	41.0	—
A_C, Å²	38.6	38.8	44.5	35.6	38.4
π_{tr}, dynes/cm	24.5	17.7	14.3	19.2	—
π_C, dynes/cm	51.3	45.0	42.2	46.6	40.2

[a] Surface parameters have the same definitions given in Table I.

35.3 dynes/cm and the transition surface pressure is decreased from 25.1 to 17.1 dynes/cm. Hence, some association with the monolayer undoubtedly occurs. At 4×10^{-5} M PGB_1, expansion of the monolayer is evident. The value of $Å_L$ is increased from 25.1 to 26.7 Å²/molecule, and the value of $Å_S$ is increased from 20.9 to 22.7 Å²/molecule. The collapse pressure is further reduced to 25.7 dynes/cm. It is particularly interesting that no plateau region is observed in the π–A plot. The data support some penetration of the monolayer by PGB_1 at the higher concentration. The absence of a plateau might result from additional configurational constraints placed on PGB_1 molecules as a result of the more rigid, conjugated dienone system formed by the C_{8-12} double bond with the C_{12} side-chain double bond at C_{13} and the keto function at C_9. This could conceivably impose configurational requirements on the molecule such that the C_{12} side chain and cyclopentanone ring are constrained to limited positions within the surface. The observed instability following penetration of the monolayer at the higher PGB_1 concentration would then be attributed more to a disruptive effect upon monolayer structure and packing rather than to any specific interaction with the film species. The relative order of surface activities observed for the four prostaglandins in terms of increasing monolayer instability, as reflected by reductions in collapse surface pressure, $\Delta\pi_c$ (Table I), is $PGA_1 > PGF_{2\alpha} \approx PGE_2 \approx PGB_1$ at 2×10^{-5} M. These activities are delineated more clearly at the higher concentration, with $PGA_1 > PGB_1 > PGF_{2\alpha} > PGE_2$.

Cholesterol monolayers can provide a useful system for acquiring insight into the possible types of interactions that may be involved with the prostaglandin compounds. Intermolecular hydrogen bonding was suggested as one primary type of interaction involved in expansion of stearic acid monolayers and, if such is the case, the effect should be accentuated with cholesterol monolayers. Figures 5 and 6 depict π–A plots obtained for cholesterol monolayers spread on PGE_2 and $PGF_{2\alpha}$ subphases, respectively. The surface parameters are summarized in Table II. In each case, increased film instability occurs with an increasing concentration of prostaglandin, as evidenced by the decreases in collapse surface pressure (Table II). This surface behavior is in general agreement with similar effects observed for the two prostaglandins on stearic acid monolayers (Figs. 1 and 2 and Table I). A comparison of Figs. 5 and 6 illustrates the importance of the polar functions of the ring system, especially the hydroxyl group at C_9 in $PGF_{2\alpha}$. The cholesterol monolayer spread on 4×10^{-5} M $PGF_{2\alpha}$ is significantly expanded in the initial region of the π–A isotherm. This can be contrasted to the minimal expansion observed for cholesterol with PGE_2 at 4×10^{-5} M. $PGF_{2\alpha}$ molecules appear capable of film penetration, as was observed for stearic acid monolayers; but, in addition to penetration, $PGF_{2\alpha}$ apparently can effectively hydrogen bond with the hydroxyl group of cholesterol. The interaction results in an appreciably more expanded film, with increased surface pressure development occurring in the initial regions of the isotherm.

Another comparison is illustrated in Figs. 7 and 8 for the surface behavior for these two prostaglandins, using distearoyl phosphatidic acid monolayers. This system has a larger polar moiety than stearic acid or cholesterol and, at the same time, presents a rigid hydrophobic character to the prostaglandin molecules. It can be observed from the figures that PGE_2 and $PGF_{2\alpha}$ exhibit surface behavior similar to that observed in the case of the stearic acid mo-

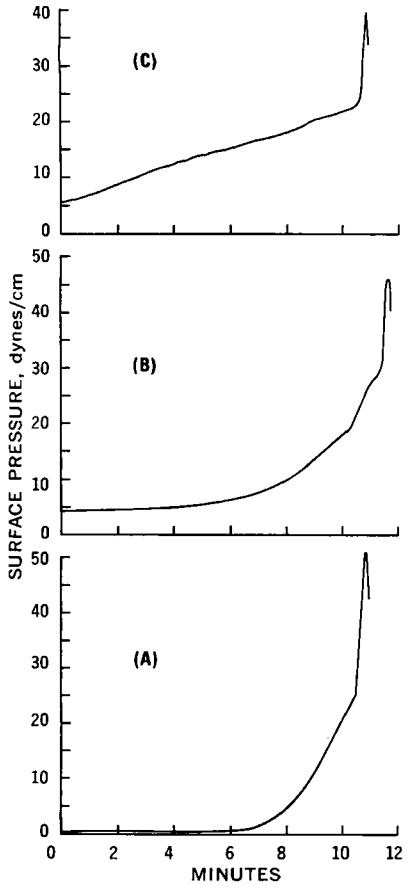


Figure 8—*The π–A compression curves for distearoyl phosphatidic acid monolayers spread on (A) 0.01 M HCl, (B) 0.01 M HCl with 2.0 × 10⁻⁵ M PGF₂α, and (C) 0.01 M HCl with 4.0 × 10⁻⁵ M PGF₂α. Area per molecule at zero time is 75.9 Å²; V₀ = 3.45 Å²/molecule/min.*

nolayers. PGE_2 causes minimal expansion of the monolayer but, nevertheless, increased instability, as evidenced by reductions in the transition and collapse surface pressures (Table III). $PGF_{2\alpha}$ brings about significant expansion of the distearoyl phosphatidic acid monolayers, with increased instability, and this is again similar to its effect on both stearic acid and cholesterol monolayers. Hence, no major differences in surface behavior of the two prostaglandins can be observed when stearic acid is replaced by a molecule having two C_{18} alkyl chains. One can conclude from this important observation that hydrophobic interactions within the film are not sufficient to counteract instability created in the monolayer by polar group interactions with the prostaglandin molecules.

In conclusion, all four of the naturally occurring prostaglandins investigated bring about increased instability in monomolecular films of stearic acid when dissolved in the aqueous subphase at very low concentrations. The relative order of surface activities is $PGA_1 > PGB_1 > PGF_{2\alpha} > PGE_2$. PGE_2 does not appear to penetrate the monolayer readily but apparently can associate with the polar groups of the film, bringing about instability. PGB_1 forms a mixed monolayer system with stearic acid and exhibits a disruptive effect upon monolayer structure that leads to increased film instability. Both $PGF_{2\alpha}$ and PGA_1 cause significant expansion in the π–A isotherms for stearic acid and appear capable of occupying area-determining positions within the surface. In addition, $PGF_{2\alpha}$, which has hydroxyl groups at C_9 and C_{11}, can effectively hydrogen bond with stearic acid molecules. This effect is accentuated when stearic acid is replaced by a cholesterol monolayer. Comparison of the π–A isotherms obtained for stearic acid and distearoyl phosphatidic acid monolayers did not indicate any significant differences in surface effects for the film penetrant $PGF_{2\alpha}$ or the PGE_2 molecule. Both prostaglandins showed similar behavior to that observed in the case of the stearic acid monolayer. From these findings, it is concluded that the primary instability created in the film resides within the polar groups of the film-forming molecules.

Surface activities for $PGF_{2\alpha}$ and PGE_2 follow the same order as that observed for F- and E-type prostaglandins in inhibition of sodium flux across the intestinal mucosa (8). However, this order is just the reverse of their uterine-stimulating activity observed for the pregnant human uterus (22). Such differences emphasize the multiplicity of actions which may be attributable to these compounds biologically and the inherent pitfalls involved in making any rash extrapolations to biological systems. However, the surface activities for PGA_1 and PGB_1 do follow closely the *trend* of biological depressor activity reported by Jones (23) for lowering cat and dog blood pressure after intraaortic injection, *i.e.*, $PGA_1 \gg PGB_1$. In addition, PGA_1 was observed to exhibit biphasic activity. Such activity parallels the dual role observed for PGA_1 in destabilization of stearic acid monolayers at the low and high concentration levels. However, more evidence is required to substantiate any extrapolations of the surface data toward mechanistic considerations for biological action of the prostaglandins.

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* Undergraduate research assistant from Xavier University with the Pharmacy Research Unit of The Upjohn Co., summer 1973.

ˣ To whom inquiries should be directed.