Platelet-Activating Factor Mediates Angiotensin II-Induced Proteinuria in Isolated Perfused Rat Kidney

NORBERTO PERICO,* † RADOSLAW LAPINSKI,* KRZYSZTOF KONOPKA,* SISTIANA AIELLO,* MARINA NORIS,* and GIUSEPPE REMUZZI* †

*Mario Negri Institute for Pharmacological Research and †Division of Nephrology and Dialysis, Ospedali Riuniti di Bergamo, Bergamo, Italy.

Abstract. Isolated kidney preparations (IPK) from male Sprague Dawley rats perfused at constant pressure were used to evaluate the effect of angiotensin II (AII) and platelet-activating factor (PAF) on renal function and urinary protein excretion. Compared with basal, intrarenal infusion of AII at 8 ng/min caused a progressive increase in protein excretion (11 ± 6 versus 73 ± 21 µg/min) in parallel with a decline in renal perfusate flow (RPF) (29 ± 3 versus 18 ± 3 ml/min). Addition to the perfusate of PAF at 50 nM final concentration also induced proteinuria (9 ± 4 versus 55 ± 14 µg/min) but did not change RPF (29 ± 3 versus 30 ± 3 ml/min). Pre-exposure of isolated kidneys to the PAF receptor antagonist WEB 2086 prevented the increase in urinary protein excretion induced by AII infusion (basal: 13 ± 6; post-AII: 12 ± 7 µg/min) but failed to prevent the vasoactive effect of AII (RPF, basal: 30 ± 2; post-AII: 21 ± 3 ml/min). In additional experiments, dexamethasone reduced the proteinuric effect of AII remarkably. These results indicate that in isolated kidney preparation: (1) AII infusion induced proteinuria and decreased RPF; and (2) the effect of AII in enhancing urinary protein excretion was completely prevented by a specific PAF receptor antagonist, which, however, did not influence the AII-induced fall in RPF. It is suggested that PAF plays a major role in AII-induced changes in the permselective function of the glomerular capillary barrier. (J Am Soc Nephrol 8: 1391–1398, 1997)

Received October 28, 1996. Accepted March 28, 1997.
Correspondence to Dr. Norberto Perico, Mario Negri Institute for Pharmacological Research, Via Gavazzeni 11, 24125 Bergamo, Italy.
Dr. Timothy Meyer served as Guest Editor and supervised the review and final disposition of this manuscript.

1046-6673/0809-1391$03.00/0
Journal of the American Society of Nephrology
Copyright © 1997 by the American Society of Nephrology
Animals could be dissociated by the effect on membrane permeability conducted in accordance with institutional guidelines in compliance essential for such studies. The aim of the present investigation was to determine what extent All-induced changes in glomerular permeability to macromolecules involved the PAF pathway and whether their respective influence on determinants of renal hemodynamic could be dissociated by the effect on membrane permeability properties.

**Materials and Methods**

**Animals**

Adult male Sprague Dawley rats (Charles River, Italia SpA, Calco, Italy) were used in the studies. Animal care and treatment were conducted in accordance with institutional guidelines in compliance with national and international laws and policies (European Economic Community Council Directive 86/609, OJL 358, December 1987; National Institutes of Health Guide for the Care and Use of Laboratory Animals, National Institutes of Health Publication No. 85-23, 1985). All animals were allowed free access to standard rat chow and tap water.

**Experimental Design**

To compare the effect of All and PAF on glomerular permeability to macromolecules, isolated kidneys were perfused in a recirculating system at a constant pressure of 100 mmHg with an artificial cell-free medium. Each kidney was allowed 15 to 20 min to equilibrate after beginning the perfusion. A 10-min baseline urine collection and a perfusate sample were obtained at the end of the control clearance period. Then in a group of isolated kidneys (group 1, n = 8), PAF (final concentration, 50 nM; Bachem-Feinchemikalien, Bubendorf, Switzerland) was added to the perfusate reservoir, and five consecutive 10-min experimental clearance periods were performed. Addition of PAF to the perfusate was done according to our previous studies showing the efficacy of this approach in inducing proteinuria in IPK (22); pilot experiments in IPK allowed us to establish the final concentration of PAF in the perfusate that gives comparable proteinuric effect to that of 8 ng/min infusion of All. In another group (group 2, n = 10), after basal clearance period, a continuous infusion of All (8 ng/min) into the renal artery was started, and five consecutive clearances were performed. This dose has been shown previously to enhance urinary protein excretion rate in IPK (18). Moreover, we have chosen to infuse All into the renal artery because of the very transient hemodynamic effect when the hormone was given as a single intravenous injection, at least in IPK (30). As a control group (group 3, n = 6), the vehicle in which All was dissolved was continuously infused into the renal artery as in the group 2 experiments. For each collection period, urine and venous effluent samples were analyzed for creatinine concentration. GFR, renal perfusate flow (RPF), filtration fraction (FF), urine output, and urinary protein excretion rate were evaluated throughout the experiment.

To investigate whether the possible changes in glomerular permeability to macromolecules induced by All are the consequences of its direct effect on glomerular capillary barrier or whether the changes are mediated by stimulation of intraglomerular synthesis of PAF, additional experiments were performed in the presence of PAF receptor antagonist. After the equilibration period, the PAF receptor antagonist WEB 2086 (Boehringer Ingelheim KG, Ingelheim am Rhein, Germany) (31) at the final concentration of 10 μM (n = 10) or its vehicle (n = 6) was added to the perfusion fluid. Ten minutes later, a continuous infusion of All (8 ng/min) into the renal artery was started, and five consecutive clearance periods were performed. Renal function parameters and urinary protein excretion rates were measured during each clearance period. WEB 2086 is the most widely studied PAF antagonist of the hexatetrazepine series (32). It is a thieno-triazolo-diazepine 3{-4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f][1,2,4]-triazolo-[4,3-a][1,4]-diazepine-2-y1]-1-(4-morpholinyl)-1-propanone, which has PAF antagonistic activity in the active and passive anaphylaxis (33) and the endotoxic shock (34). The selectivity of the compound has been documented previously by the fact that, in the rabbit skin, WEB 2086 inhibited the vascular leakage to PAF but did not affect edema responses to bradykinin, histamine, formylmethionylleucylphenylalanine, C5a, LTB4, and zymosan (35). Moreover, WEB 2086 inhibited PAF-induced platelet aggregation in a concentration-dependent manner, but had little or no effect on the aggregation induced by ADP, epinephrine, collagen, and arachidonic acid (31). The dose of WEB 2086 has been chosen according to previous studies showing the ability of the compound to specifically inhibit PAF-induced platelet and neutrophil aggregation in vitro, and bronchoconstriction, systemic hypotension, and lethal effects due to intravenous PAF infusion in guinea pigs, as well as vascular permeability induced by PAF in the rat skin (31).

To evaluate whether the proteinuric effect of PAF is the result of its action on the cytoskeleton of podocytes, additional experiments were performed pre-exposing kidneys to dexamethasone. Rats were treated with dexamethasone (1.25 mg/kg, intraperitoneally) 3 h before surgery. Then, dexamethasone (1 μM, n = 6) was added to the perfusion solution. This dose of the glucocorticoid has been reported previously to stabilize the actin cytoskeleton of several cell types in vitro (36). After the equilibration period and 10-min basal clearance, PAF (50 nM, final concentration) was added to the perfusate, and five consecutive 10-min experimental clearance periods were performed. As a control, the same experimental design was followed except that vehicle (n = 5) was used instead of dexamethasone. Renal function parameters and urinary protein excretion were measured during each clearance period.

**Perfusion Procedure and Apparatus**

The perfusion technique used in these experiments has been described previously in detail (22). Briefly, rats were anesthetized with thiopental sodium (50 mg/kg body wt, intraperitoneally), the abdominal cavity was exposed, and the right ureter was cannulated with PE-10 polyethylene tubing (Clay-Adams, Parsippany, NJ). A PE-240 polyethylene catheter was introduced into the vena cava below the right renal vein and secured in place. The renal artery was then cannulated with a short, blunted 19-gauge needle via the superior mesenteric artery to avoid interruption of flow to the kidney. At this time, the rat was killed. The kidney was then perfused in situ in a recirculating system with a medium held at 37°C by a constant Haake D1 temperature circulator system (Haake, Berlin, Germany) and gassed with a mixture of 95% O2, 5% CO2 through a hollow-fiber membrane oxygenator. The perfusate was delivered to the renal artery cannula through a peristaltic pump, an in-line 8-μm-pore-size filter (Sartorius, Göttingen, Germany), and a glass bubble trap.

The perfusate consisted of Krebs-Henseleit bicarbonate buffer containing 3.5 g/dl Ficol 70 (Farmacia Fine Chemical, Uppsala, Sweden), 1 g/dl bovine serum albumin (Pentex BSA Fraction V, Miles Laboratories, Elkhart, IN), 200 mg/dl glucose, 36 mg/dl urea, 50 mg/dl creatinine, and a mixture of amino acids. The total volume of the perfusate in the system was 250 ml.

Urine flow was determined gravimetrically. GFR was calculated as
creatinine clearance. This has been shown to give the same GFR estimates in the isolated perfused kidney as inulin clearance (37). RPF was determined volumetrically. The perfusion pressure was continuously measured with a Statham transducer (Gould, Düsseldorf, Germany) connected to the arterial cannula. The effective perfusion pressure (cannula tip pressure) was derived by subtracting from the measured pressure the pressure drop known to occur across the arterial cannula at a given flow, and was kept constant at 100 mmHg throughout the experiments. Therefore, changes in RPF reflected changes in renal vascular resistance. FF was estimated by the ratio GFR/RPF. Total urinary protein excretion rate was measured in duplicate samples by the Coomassie brilliant blue dye-binding assay (38).

Statistical Analyses

Results are expressed as mean ± SD. Data were analyzed using the t test for paired data or two-way ANOVA, as appropriate. The significance level of differences between individual group means, subjected to ANOVA, was established using the Tukey-Cicchetti test for multiple comparisons (39).

Results

Effect of Angiotensin II and PAF on Renal Function and Urinary Protein Excretion

In kidneys exposed to exogenous All, the urine flow rate ranged from 90 µl/min at baseline to 115 µl/min at the end of the 50-min continuous infusion of the hormone into the renal artery. The urine output of isolated kidneys challenged with PAF was also in the same range (95 to 122 µl/min). These values were not significantly different from those in kidneys exposed to vehicle alone (89 to 114 µl/min).

Table 1 shows the effect of All or PAF on GFR. All infusion caused a progressive decline in GFR compared with basal values, but the difference did not reach statistical significance. A tendency to GFR reduction was also observed when kidneys were challenged with PAF, despite the fact that, numerically, this phenomenon was less pronounced than with All. When kidneys were exposed to vehicle, the decline in GFR was minimal during the 50-min perfusion and was comparable to that found with PAF. However, GFR did not differ significantly between the three experimental groups at any time point considered.

As shown in Table 2, RPF was reduced during All infusion and reached statistical significance 20 min after exposure of the kidney to the vasoactive peptide compared with preinfusion values. By contrast, after the addition of PAF to the perfusate, RPF remained quite constant during the entire experimental period and at values comparable to baseline RPF. Similarly, the infusion of vehicle into the renal artery did not cause any significant change of RPF values. Considering differences between groups, RPF was significantly lower during exposure of isolated kidneys to All than to PAF or vehicle. All infusion, but not PAF or vehicle, significantly enhanced the FF compared with baseline values (Table 3).

Figure 1 shows the effect of All and PAF on urinary protein excretion rate. Basal protein excretion rates remained constant before kidney exposure to All, PAF, or vehicle and were comparable in the three groups of isolated kidneys. The infusion of All induced a progressive increase in proteinuria over the basal values that was sixfold higher than baseline values at the end of the study period. The exposure of kidneys to PAF also resulted in an approximately sixfold increase in urinary protein excretion over basal values. Urinary protein excretion was not significantly different in kidneys challenged with All and PAF. When kidneys were infused with vehicle, the urinary protein excretion rate remained constant during the entire observation period.

Effect of a Specific PAF Receptor Antagonist

Exposure of isolated kidneys to WEB 2086, a selective PAF receptor antagonist, had no influence on basal renal function, as indicated by lack of change in GFR, RPF, and FF, compared with its vehicle during the first 10-min perfusion (Table 4). Addition of WEB 2086 to the perfusate did not prevent the progressive decline in GFR induced by All infusion. Indeed, at the end of the observation period (50 min after starting the infusion of the vasoactive peptide), GFR values were comparable to those obtained in kidney exposed to vehicle and continuously infused with All (Table 4).

A 31 and 36% decline in RPF was observed during All infusion of kidneys pre-exposed to the PAF receptor antagonist and its vehicle, respectively (Figure 2 and Table 4). Similarly, a comparable increase in FF was documented in the two groups of isolated perfused kidneys (Table 4).

In preliminary experiments, we found that WEB 2086 added to the perfusate at 10 µM final concentration almost completely prevented PAF-induced proteinuria in isolated kidneys (WEB 2086 plus PAF: 11.3 ± 4.8 µg/min; PAF: 60.5 ± 10.5

| Table 1. Effect of All or PAF on GFR in isolated perfused rat kidneys* |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Group           | 10 min**        | 20 min          | 30 min          | 40 min          | 50 min          | 60 min          |
|                 | GFR (ml/min)    | GFR (ml/min)    | GFR (ml/min)    | GFR (ml/min)    | GFR (ml/min)    | GFR (ml/min)    |
| Vehicle         | 0.89 ± 0.15     | 0.88 ± 0.16     | 0.84 ± 0.16     | 0.79 ± 0.18     | 0.75 ± 0.17     | 0.71 ± 0.18     |
| All (8 ng/min)  | 0.97 ± 0.16     | 0.84 ± 0.19     | 0.78 ± 0.23     | 0.67 ± 0.19     | 0.65 ± 0.16     | 0.61 ± 0.13     |
| PAF (50 nM)     | 0.92 ± 0.23     | 0.93 ± 0.25     | 0.89 ± 0.19     | 0.91 ± 0.22     | 0.91 ± 0.24     | 0.82 ± 0.27     |

*Values are mean ± SD. All, angiotensin II; PAF, platelet-activating factor.

**Baseline preinfusion values. There is no statistical difference between groups at any time points.


Table 2. Effect of All or PAF on RPF in isolated perfused rat kidneys

<table>
<thead>
<tr>
<th>Group</th>
<th>RPF (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 min&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Vehicle</td>
<td>30 ± 2</td>
</tr>
<tr>
<td>All (8 ng/min)</td>
<td>29 ± 3</td>
</tr>
<tr>
<td>PAF (50 nM)</td>
<td>29 ± 3</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values are mean ± SD. RPF, renal perfusate flow. Other abbreviations as in Table 1.

<sup>b</sup> Baseline preinfusion values.

<sup>c</sup> P < 0.01 versus basal values.

Table 3. Effect of All or PAF on FF in isolated perfused rat kidneys

<table>
<thead>
<tr>
<th>Group</th>
<th>FF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 min&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Vehicle</td>
<td>0.031 ± 0.004</td>
</tr>
<tr>
<td>All (8 ng/min)</td>
<td>0.030 ± 0.002</td>
</tr>
<tr>
<td>PAF (50 nM)</td>
<td>0.032 ± 0.007</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values are mean ± SD. FF, filtration fraction. Other abbreviations as in Table 1.

<sup>b</sup> Baseline preinfusion values.

<sup>c</sup> P < 0.05 versus basal values.

Figure 1. Effect of angiotensin II (All) or platelet-activating factor (PAF) on urinary protein excretion rate in isolated perfused rat kidneys. Values are mean ± SD. *P < 0.01 versus basal (pre-All, PAF, or vehicle, 10 min).

µg/min, P < 0.01). As shown in Figure 2, in the presence of WEB 2086 (10 µM), urinary protein excretion rate did not increase after kidneys were perfused with All. Thus, in these isolated kidneys, the protein excretion rate during All infusion was comparable to preinfusion values (basal: 13.0 ± 6.7 µg/min; All: 12.3 ± 7.5 µg/min). On the other hand, infusion of All into the renal artery of kidneys pre-exposed to vehicle progressively enhanced the urinary protein excretion rate (Figure 2).

Effect of Dexamethasone on PAF-Induced Proteinuria

As shown in Table 5, pre-exposure of isolated kidneys to dexamethasone had no influence on basal GFR, RPF, and FF, compared with its vehicle during the first 10-min perfusion. Addition of PAF to the perfusate in the presence of dexamethasone or vehicle did not result in any significant change in renal function.

Figure 3 shows the effect of dexamethasone or its vehicle on PAF-induced proteinuria. In isolated kidneys exposed to vehicle and challenged with PAF, a progressive increase in urinary protein excretion rate was found. On the other hand, pretreatment of kidneys with dexamethasone markedly, but not completely, prevented the increase in protein excretion induced by adding PAF in the perfusion solution.

Discussion

We have documented that All infusion into the renal artery, as well as addition of PAF to the perfusate, increased glomerular permeability to proteins and caused proteinuria in the isolated perfused rat kidney preparation. At the dose of the two exogenous stimuli used, the time course and the degree of development of proteinuria were comparable. The same effect on urinary proteins, however, was observed with clear differences in the hemodynamic effect of the two molecules. Actually, All reduced RPF and increased FF, whereas PAF did not change RPF and FF. We have also found that in the same preparation, blockade of PAF activity at receptor level with WEB 2086 completely prevented the increase in urinary pro-
Table 4. Effect of PAF receptor antagonist on changes in renal function induced by All infusion

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle</th>
<th>WEB 2086</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Post-All</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>0.97 ± 0.19</td>
<td>0.69 ± 19</td>
</tr>
<tr>
<td>RPF (ml/min)</td>
<td>29 ± 3</td>
<td>19 ± 3&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>FF</td>
<td>0.030 ± 0.02</td>
<td>0.035 ± 0.02&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values are mean ± SD.
<sup>b</sup> Baseline preinfusion values.
<sup>c</sup> *P* < 0.01 versus basal values.
<sup>d</sup> *P* < 0.05.

Recorded during the infusion of the hormone was not influenced by the receptor antagonist.

These findings suggest that PAF mediated most of the effects of All on glomerular permeability properties to macromolecules, without influencing the renal vasoconstrictory properties of the peptide. Previous in vivo studies in rats have shown that All-induced proteinuria involves changes in the sieving properties of the glomerular capillary wall (17,40). The sieving defect induced by All has been explained, in large part, by the capacity of the hormone to increase intraglomerular capillary pressure, thus modulating transmural hydraulic pressure, which, in turn, reflects its ability to regulate efferent arteriolar vasoconstrictor tone. Our findings in IPK might not necessarily apply to the in vivo conditions, but they do provide direct evidence that All can enhance glomerular membrane permeability to proteins by mechanism(s) not solely related to changes in convective or diffusive forces, or both, across the membrane as a result of the hemodynamic effects of the hormone. In this respect, it should be noted that the isolated perfused rat kidney has become recognized as a suitable preparation for the study of many physiological and biochemical aspects of renal function (41,42). This is a relatively simple technique in which variables can be changed in a controlled manner and systemic influences on renal function can be eliminated. These features should be balanced, however, against functional abnormalities that persist even in the best isolated kidney preparations. Altered hemodynamic characteristics, impaired urinary concentrating and diluting ability, and, in general, abnormal distal nephron functions are the prominent deficiencies of the preparation. On the other hand, glomerular and convoluted proximal tubule functions are well preserved.

Taken together, these results suggest that All modulates glomerular membrane permeability properties in a complex way that involves both hemodynamic and nonhemodynamic factors.

How PAF can alter glomerular permeability to proteins remains unclear. The glomerular filtration barrier is a complex microvascular structure composed of an endothelium with large open pores, a specialized glomerular basement membrane, and narrow slits located between the interdigitating processes of the podocytes (43). It is now generally accepted that glomerular basement membrane and epithelial cell slight

![Figure 2. Effect of pretreatment with the PAF receptor antagonist WEB 2086 on All-induced decline in renal perfusate flow (RPF, Top Panel) and proteinuria (Bottom Panel) in isolated perfused rat kidney preparation. Values are mean ± SD. *P* < 0.01 versus basal (pre-All, 10 min).](image)
cytoskeleton alterations governing cell-cell interactions is sup-
ported by data showing that exposure of endothelial cells to
agents known to increase vascular permeability, including the
proteinuria in isolated perfused rat kidneys. Values are mean
± SD. (49), an inhibitor of cytoskeletal function.
In vitro experiments were conducted in the presence of cytochalasin B
shape after exposure to the latter agents were not seen when the
changes in vascular permeability and cell
(48). Moreover, both changes in vascular permeability and cell
process width, however, decreased when rats were infused with
processes have a highly developed cytoskeleton suggestive of
contractile function, it is possible that PAF may alter the
permeability changes of the glomerular barrier by mediating
contraction within the foot processes and enhancing the size of
glomerular slit pores. Recent evidence is available that glu-
corticoids, besides other effects on cells, stabilize the actin
cytoskeleton by inducing formation of cross-linked actin net-
works in a variety of cell types in culture (51) and contribute
to the formation of numerous stress fibers (36). Assuming that
doses of dexamethasone, which stabilize actin cytoskeleton in
cell culture, do the same on glomerular epithelial cells in the
isolated perfused kidney preparation, our present findings that
pre-exposure of kidney to dexamethasone markedly reduced
the proteinuric effect of PAF in the isolated perfused prepara-
tion suggest the possible contribution of podocyte cytoskeleton in
modulating the permeability change of glomerular capillary
barrier to macromolecules induced by PAF. However, one
must consider that stabilization of the cytoskeleton is only one
of the potential mechanisms of dexamethasone and that other
effects of the compound on epithelial cells may also contribute
to reducing the proteinuric effect of PAF in our in vitro system.

Because visceral epithelial cells have been shown to possess
All receptors (52), it is tempting to speculate that perme selec-
tive dysfunction of the glomerular capillary barrier induced by
All may derive from the ability of this vasoactive peptide to
stimulate formation and release of PAF from glomerular epi-
theilial cells. This phospholipid, by binding to its specific
receptors, activates a series of intracellular events that lead to
cytoskeleton alteration, resulting in shape changes of the foot
processes and ultimately widening the slit pores and enhancing
protein traffic across the glomerular capillary wall. In support
of this hypothesis are recent findings of morphometric analysis of
the effects of All on glomerular structure in rats (53). They
indeed show a tendency for increases of total length of filtrati-
sion slit overlying peripheral capillary wall per glomerulus, as
well as of mean slit width at the level of diaphragm. Mean foot
process width, however, decreased when rats were infused with
All in the left renal artery. It should be noted that values of
these parameters were numerically, but not statistically, differ-
ent compared with those in control animals. This may be due
to the fact that, indeed, All causes diffuse changes in slit
structure, but these changes are largely masked during tissue
fixation. Thus, Furukawa et al. (54) have recently reported that
perfusion fixation may cause shrinkage of foot processes.

In conclusion, our study indicates that in isolated perfused

Table 5. Effect of dexamethasone on renal function during exposure of isolated kidney to PAF (50 nM)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal</td>
<td>Post-PAF</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>0.91 ± 0.18</td>
<td>0.76 ± 0.19</td>
</tr>
<tr>
<td>RPF (ml/min)</td>
<td>29 ± 3</td>
<td>29 ± 2</td>
</tr>
<tr>
<td>FF</td>
<td>0.031 ± 0.004</td>
<td>0.029 ± 0.005</td>
</tr>
</tbody>
</table>

* Values are mean ± SD. Abbreviations as in Tables 1, 2, and 3.
kidney: (1) All and PAF increased urinary protein excretion at a comparable extent and with a similar time course; (2) All-induced proteinuria was completely prevented by a specific PAF receptor antagonist that failed to modulate the renal hemodynamic effect of the vasoactive peptide; and (3) dexamethasone markedly reduced PAF-induced proteinuria via mechanisms that remain to be established.

Acknowledgment

We thank Boehringer Ingelheim KG (Ingelheim am Rhein, Germany) for the gift of WEB 2086 through the courtesy of Dr. Giuliano Bensi.

References

33. Casals-Stenzel J: Effect of WEB 2086, a novel antagonist of...
platelet activating factor, in active and passive anaphylaxis. *Immunopharmacology* 3: 7–24, 1987


