Platelet activating factor: release from colonic mucosa in patients with ulcerative colitis and its effect on colonic secretion

T D Wardle, L Hall, L A Turnberg

Abstract

Inflammatory mediators have been implicated in the pathophysiology of ulcerative colitis. They may stimulate intestinal secretion and contribute to the production of diarrhoea. Platelet activating factor (PAF) may be responsible for a high proportion of this secretory response. Biopsy specimens from inflamed and quiescent mucosa of patients with ulcerative colitis and normal human colonic mucosa were cultured or co-cultured. The release of PAF, prostaglandin E2, and leukotriene D4 into the culture medium was measured and the ability of this culture medium, from inflamed and normal tissues, to influence secretion in rat colonic mucosa was assessed. PAF was liberated by inflamed tissue. Its release from quiescent but not normal tissue was stimulated by medium in which inflamed mucosal biopsy tissues had been cultured and by exogenous bradykinin and 5-hydroxytryptamine, but not by histamine. PAF stimulated eicosanoid production. The rise in short circuit current produced in vitro by inflamed tissue culture medium was inhibited by the PAF receptor antagonist (CV-6209) (46%) (32-4 (2-9) v 17-5 (1-19) μA.cm⁻², p<0.005) and further by combined cyclooxygenase and lipooxygenase inhibition (indomethacin plus ICI 207968) (58%) (32-4 (2-9) v 13-6 (1-9) μA.cm⁻², p<0.005). Mepacrine and hydrocortisone attenuated considerably the electrical response evoked by medium from inflamed mucosa to a similar extent (32-4 (2-9) v 6-3 (1-2) v 5-1 (0-9) μA.cm⁻², p<0.001). These data suggest that PAF accounted for 46% of the culture medium secretory effect. Thus, any attempt to block its release in patients with ulcerative colitis may have only a partial effect on their symptoms.

Keywords: arachidonic acid, phospholipase A2, cyclooxygenase, lipooxygenase, eicosanoid, prostaglandin E2, leukotriene D4, platelet activating factor.

Platelet activating factor (PAF) is derived predominantly from membrane bound phosphatidylcholine. It is rapidly synthesised after activation of inflammatory cells and has been found in high concentrations in colonic mucosal biopsy tissue from patients with ulcerative colitis. PAF exhibits a variety of effects, in particular on inflammatory cells. These effects are mediated via specific plasma membrane receptors and include modulation of the immune response by stimulating the production of other mediators, vasodilation, increased vascular permeability, and the promotion of chemotaxis. PAF also stimulates mucosal chloride secretion and inhibits sodium chloride absorption, so it could contribute to the production of diarrhoea in ulcerative colitis. During the inflammatory response, however, many mediators are released and it is difficult to establish which is responsible for liberating PAF and which, if any, is responsible for mediating its effect on mucosal function.

We previously reported that culture medium from inflamed colitic mucosa evoked a secretory response that was partly mediated by arachidonic acid metabolites - that is prostaglandins and leukotrienes. Because inhibitors of these arachidonic acid metabolites failed to block all of the secretory effect, we postulated that another phospholipid derivative, PAF, might account for the remaining secretory response. To test this hypothesis we have investigated factors that influence the release of PAF from human colonic mucosa, examined its effect on colonic secretion and considered whether this effect is mediated by prostaglandins and leukotrienes.

Methods

PATIENT DETAILS

Mucosal biopsy specimens were taken from 40 patients during colonoscopy. All had undergone bowel preparation consisting of a three day low residue diet and, one day before the examination, a combination of X prep (purified senna extract; 1 ml/kg body weight) and 10% mannitol (500 ml) modified according to the patients’ symptoms.

Twenty eight patients (16 M, 12 F, median age 38.3 years) with active proctosigmoiditis (grade 3/4) had biopsy specimens taken from inflamed rectal mucosa and also from uninflamed, 'quiescent' proximal mucosa from the ascending colon. At the time of colonoscopy nine patients were taking mesalazine (400 mg three times daily), six predisolone (5 to 15 mg once daily), and 10 topical steroids. Twelve patients (6 M, 6 F, median age 36.8 years), who were being investigated for altered bowel habit, had biopsy specimens taken from endoscopically and histologically normal colonic...
mucosa. To minimise tissue trauma all biopsies were taken with non-snipped forceps.

**BIOPSY CULTURE**

After removal, mucosal biopsy specimens were immediately placed in transport medium (L15, with added penicillin G 100 units/ml and streptomycin sulphate 100 µg/ml); transferred to the laboratory; gently washed three times in the L15 medium; and carefully blotted, weighed, and placed in a 4 cm culture dish containing 1 ml of culture medium (CMRL 1066, plus glucose 5 µg/ml, methionine 1 µg/ml, Tris buffer 20 mM, glutamine 3 mM, β-retinyl acetate 1 µg/ml, penicillin G 100 units/ml, streptomycin sulphate 100 µg/ml, gentamicin 50 µg/ml, and amphotericin β 0·25 µg/ml).

**Isolated biopsy culture**

Biopsy specimens from inflamed, quiescent, and normal mucosa were cultured to assess PAF release.

To investigate the effect of other compounds on PAF release, specimens were cultured in the presence of one of the following:

- PAF receptor antagonist (CV6209) at a final concentration of 10⁻⁸ M.
- Potential stimulators of PAF release – bradykinin, 5-hydroxytryptamine, or histamine added to the culture medium, producing final concentrations ranging from 10⁻⁸ to 10⁻⁴ M. Their respective receptor antagonists des arg leu bradykinin (10⁻⁸ M), ketanserin (10⁻⁸ M), and combined chlorpheniramene maleate and ranitidine (10⁻⁶ M) were added to a further set of cultures.
- Potential inhibitors of PAF release – mepacrine and hydrocortisone (phospholipase A₂ inhibitors) 10⁻⁵ M.
- Potential PAF effectors – prostaglandin and leukotrienes release was inhibited by a combination of indomethacin and ICI 207968 (10⁻⁵ M) (cyclooxygenase and lipooxygenase inhibition, respectively).
- Combination of indomethacin, ICI 207968, and CV 6209 (combined cyclooxygenase and lipooxygenase inhibition, plus PAF receptor antagonist) all at a concentration of 10⁻⁵ M.

**Co-culture**

Mucosal biopsy specimens from either inflamed, 'quiescent', or normal tissue were co-cultured in various paired combinations in a 4 cm dish divided by a polypropylene barrier. This was designed, as described previously, to allow free circulation of culture medium and to prevent direct tissue contact between the two biopsy specimens.¹⁵

All culture dishes were placed in a humidified chamber maintained at 37°C, supplied with a mixture of 95% O₂/5% CO₂, and rotated at 10 cycles/min. After four hours of culture the medium was removed and divided into two aliquots. One was used for measurement of inflammatory mediator production (PAF, PGE₂, LTD₄) and the other for studies of mucosal transport.

**INFLAMMATORY MEDIATOR MEASUREMENT**

**PAF**

PAF was measured by commercially available radioimmunoassay kit (Amersham, Aylesbury, Bucks, UK). Performance characteristics of this assay in our laboratory were as follows: intra-assay and interassay coefficient of variation 4% and 7% respectively, recovery 91%, sensitivity 0.1 ng/ml. Cross reactivity <0·6% for arachidonic acid, phosphatidylcholine and lyso PAF (Amersham, personal communication). All results were expressed as fmol/mg wet tissue weight/h.

**Eicosanoids**

PGE₂ and LTD₄ were measured using commercially available radioimmunoassay kits (PGE₂ du Pont, UK, Stevenage, Herts, UK; LTD₄, Amersham) as previously described.¹⁴ Performance characteristics of these assays in our laboratory were as follows: intra-assay and interassay coefficient of variation PGE₂ 5%, LTD₄ 8%; recovery PGE₂ 90%, LTD₄ 94%; sensitivity PGE₂ 1·9 pg/ml, LTD₄ 4·6 pg/ml. Cross reactivity: PGE₂ (non-E prostaglandin) <0·4%,¹⁶ LTD₄ (non-sulphidopeptide leukotrienes) <0·001%.¹⁷

**TRANSPORT STUDIES**

**Rat distal colon preparation**

Unfasted male Sprague-Dawley rats were killed and the distal colon was removed immediately and bathed in oxygenated buffer. A modified in vitro technique based on that of Ussing and Zerahn was used.¹⁸ Muscle layers were stripped and the two most distal pieces of mucosa were mounted as sheets between Perspex flush chambers, with a surface area of 0·64 cm² (VT Plate Ltd, Warrington, UK). Spontaneous basal transmucosal potential difference (PD) was measured on a high impedance digital voltmeter attached via fine tipped electrode bridges (3 M KCl in 3% agar). Short circuit current (Isc) was delivered via 1 M NaCl in 1% agar bridges, by silver/silver chloride electrodes. The electrodes were connected to a voltage clamp for automatic short circuiting. The clamp was corrected for fluid resistance between the PD and sensing bridges. Tissue conductance and resistance were calculated from the PD and Isc according to Ohm's law.

In this mucosal preparation, a rise in Isc and PD is associated with secretion of chloride ions and we have used this rise in electrical parameters as a proxy for anion secretion.

Both surfaces of each mucosal sheet were bathed with 5 ml of isotonic buffer containing: Na 146 mM, K 4·2 mM, Cl 125·8 mM, HCO₃ 26·6 mM, H₂PO₄ 0·2 mM, HPO₄ 1·2 mM, Ca 1·2 mM, Mg 1·2 mM, and glucose 10 mM, at pH 7·4. The bathing media were maintained at a constant temperature of 37°C and stirred and oxygenated via a bubble lift system using 95% O₂/5% CO₂.

The following compounds were added to the fluid bathing either the basolateral or the
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Apical aspect of the rat colonic mucosal preparation after electrical stability had been reached (usually 60 minutes).

- PAF: this was added to the fluid bathing stripped rat distal colon to produce a range of concentrations from 10^{-10} to 10^{-4} M. Changes in PD, Isc, and resistance were recorded.
- PAF receptor antagonist CV6209: this was added to the bathing fluid at a final concentration of 10^{-6} M, immediately before PAF at concentrations which had evoked a maximal and half maximal electrical response.
- Combined indomethacin and ICI 207968: this combination (10^{-3} M) was added to block production of prostaglandin and leukotrienes immediately before the addition of PAF (at concentrations which had evoked a maximal and half maximal electrical response).
- Culture medium: culture medium (100 μl) was added to the basolateral aspect of rat distal colonic mucosa and electrical parameters, as described above, were measured. This process was repeated using medium from biopsy specimens cultured in the presence of factors influencing the release of PAF as detailed above.

CHEMICALS
The 5 lipoxygenase inhibitor (ICI 207968) was kindly supplied by Dr R Dowell, Imperial Chemical Company, Alderley Edge, UK. The platelet activating factor receptor antagonist CV 6209 was kindly donated by Dr Tsukamoto (Takeda Chemical Industries, Osaka 532, Japan). PAF, indomethacin, mepacrine, bradykinin, des arg leu bradykinin, histamine, chlorpheniramine maleate, and 5-hydroxytryptamine were obtained from Sigma Chemical Company, Poole, Dorset, UK. Ketanserin was purchased from Janssen Biotech, Olen, Belgium.

STATISTICAL ANALYSIS
All values are expressed as the mean (SEM). Statistical comparisons were performed using paired or unpaired t tests. Two tailed p values were used throughout.

Results

PAF PRODUCTION
Inflamed tissue cultured in isolation produced 795 (45) fmol of PAF/mg wet tissue weight/h. PAF was not detectable in the medium from either quiescent colitic or normal mucosa (<26 fmol PAF/mg wet tissue weight/h).

Factors influencing PAF production
- PAF (10^{-9} M) added to inflamed mucosa liberated significantly less PAF than expected (1+exogenous PAF: actual: 1314 (106) v expected: 1795, p<0.01).
- PAF receptor antagonist (CV6209); basal production of PAF was not influenced by its receptor antagonist (basal: 795 (45) v 792 (49), NS) (Fig 1).
- Histamine: Histamine, ranging from 10^{-10} to 10^{-4} M, did not significantly influence PAF production by inflamed mucosa (Fig 2). Histamine did not stimulate PAF production by either quiescent colitic or normal tissue.
- Bradykinin receptor antagonist: basal PAF production by inflamed tissue was attenuated by the bradykinin receptor antagonist des-arg-leu-bradykinin (basal: 794 (45) v 494 (28), p<0.005) (Fig 1).
- Histamine receptor antagonists: basal PAF production by inflamed tissue was not significantly influenced by histamine receptor antagonists (795 (45) v 763 (49), respectively, NS) (Fig 1).
- 5-Hydroxytryptamine: this stimulated PAF production by inflamed mucosa (maximal response at 10^{-6} M 923 (58) v basal 795 (45), p<0.01) and by quiescent colitic (169 (18) v basal 0), but not normal tissue (Fig 2).
- Ketanserin attenuated PAF release by inflamed mucosa (563) (21) v 795 (45): p<0.005) (Fig 1).

Figure 1: The effect of receptor antagonists on platelet activating factor (PAF) production by cultured inflamed colonic mucosa (mean (SEM)). I=inflected, PAFrA=PAF receptor antagonist; BKrA=bradykinin receptor antagonist; HrA=histamine receptor antagonist; HTcrA=5HT receptor antagonist; CrA=combined BKrA+HrA+HTcrA; *Significantly different from basal value (p<0.01).

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tissue was not significantly influenced by combined cyclooxygenase and lipoxygenase inhibition (795 \( \times 10^{-7} \) M) and PAF generated a parallel increase in PD and a modest rise in tissue conductance. When added to the apical aspect, PAF did not evoke any electrical response. Thus, in subsequent experiments PAF was only added to the basolateral aspect of rat colonic mucosa.

Factors influencing the PAF evoked electrical response

- While pretreatment with the PAF receptor antagonist CV6209 did not significantly influence the basal Isc, it did prevent the PAF evoked increase in Isc (basal 48.9 \( \pm \) 4.3 \( \mu \text{Acm}^{-2} \)) with either quiescent or normal tissue (Figs 4 and 5).
- Pretreatment of the basolateral surface of rat colonic mucosa with both cyclooxygenase and lipoxygenase inhibitors virtually abolished the electrical response, when compared with the basal Isc (8.3 \( \pm \) 1.6 \( \mu \text{Acm}^{-2} \)), \( p<0.001 \). Basolateral addition of cyclooxygenase and lipoxygenase inhibitors significantly attenuated the short circuit response to platelet activating factor at maximal and half maximal concentrations (714 \( \times 10^{-7} \) M).

Effect of culture medium on electrical response

Medium from inflamed tissue, applied to the basolateral half chamber, generated a significantly greater Isc than medium from either quiescent or control tissue (32.4 \( \pm \) 2.7 \( \mu \text{Acm}^{-2} \), \( p<0.001 \)). Freshly prepared culture medium did not evoke any change in baseline electrical activity (Fig 7). Effect of culture medium from tissue treated with combined cyclooxygenase and lipoxygenase inhibitors. There was no significant difference between the Isc responses evoked by culture media from normal tissue that were either

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**Reactions between PAF and eicosanoids**

Inflamed tissue produced significantly more PGE\(_2\) and LTD\(_4\) than either quiescent or normal tissue (Figs 4 and 5). Exogenous PAF stimulated a concentration-dependent increase in the production rates of PGE\(_2\) and LTD\(_4\) by inflamed, quiescent, and normal tissues, with a maximum response at \( 10^{-6} \) M (Figs 4 and 5).

**Plaque activating factor (PAF) production (fmol/mg wet tissue/h) by a series of co-cultures**

<table>
<thead>
<tr>
<th>Co-culture</th>
<th>PAF production (fmol/mg wet tissue/h)</th>
</tr>
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<tbody>
<tr>
<td>C+C</td>
<td>-</td>
</tr>
<tr>
<td>Q+Q</td>
<td>-</td>
</tr>
<tr>
<td>I+I</td>
<td>828 (74)</td>
</tr>
<tr>
<td>I+C</td>
<td>341 (35)</td>
</tr>
<tr>
<td>I+C (calc)</td>
<td>358</td>
</tr>
<tr>
<td>I+Q</td>
<td>558 (40)*</td>
</tr>
<tr>
<td>I+Q (calc)</td>
<td>366</td>
</tr>
</tbody>
</table>

C=control; Q=quiescent; I=inflamed; calc=calculated; \(*=significantly\) different from calculated value \( p<0.001 \).

\( n=10 \) co-cultures/each combination.

**PAF concentration response curve**

When added to the fluid bathing the basolateral aspect of rat colonic mucosa, PAF produced a rapid increase in Isc which exhibited a biphasic response peaking after 5 and 16 minutes (Fig 6). The concentration response curve for PAF gave an EC\(_{50}\) of \( 3\times10^{-7} \) M. PAF generated a parallel increase in PD and a modest rise in tissue conductance.

**Figure 2: The effect of agonists on platelet activating factor (PAF) production by cultured colonic mucosa (mean (SEM)). I=inflamed; BK=bradykinin; H=histamine; SHT=5-hydroxytryptamine. \(*=significantly\) different from basal value \( p<0.01 \); \( \dagger=significantly\) different from basal value \( p<0.001 \).**

**Figure 3: The influence of inhibitors on platelet activating factor (PAF) production by cultured inflamed colonic mucosa (mean (SEM)). I=inflamed; CO=cyclooxygenase inhibitor; LO=lipoxygenase inhibitor; MEP=mepacrine; HC=hydrocortisone. \(*=significantly\) different from basal value \( p<0.001 \).**
untreated or exposed to combined cyclooxygenase and lipoxygenase inhibition (7-1 (0-9) v 6-7 (1), \( \mu \text{AcM}^{-2} \), NS) (Fig 7). Similar results were obtained with media from quiescent tissue, either untreated or exposed to combined cyclooxygenase and lipoxygenase inhibition (Fig 7). Culture medium from inflamed tissue treated in the same way, however, produced a significantly lower Isc when compared with medium from untreated inflamed mucosa (13-6 (1-9) v 32-4 (2-7), \( \mu \text{AcM}^{-2} \), p<0-005).

**Effect of culture medium from tissue treated with PAF receptor antagonist.** CV 6209 did not influence the modest rise in electrical activity seen with medium from either normal or quiescent biopsies (Fig 7). However, medium from inflamed tissue cultured in the presence of CV 6209 produced a significantly lower Isc than medium from untreated inflamed mucosa (17-5 (1-9) v 32-4 (2-9), \( \mu \text{AcM}^{-2} \), p<0-005).

**Effect of culture medium from tissue treated with phospholipase A_2 inhibitors.** Culture medium from normal mucosa treated with either mepacrine or hydrocortisone produced an Isc which was significantly lower than medium from either untreated tissue or from tissue exposed to combined cyclooxygenase and lipoxygenase inhibition (3-4 (0-4): 3-2 (0-3) v 7-1 (0-9): 6-7 (1), \( \mu \text{AcM}^{-2} \), respectively, p<0-01) (Fig 7). Similar results were obtained with culture medium from quiescent tissue. Medium from inflamed tissue treated with either mepacrine or hydrocortisone produced a significantly lower Isc than medium from either untreated or from tissue exposed to combined cyclooxygenase and lipoxygenase inhibition (6-3 (1-2): 5-1 (0-9) v 32-4 (2-7): 13-6 (1-9), \( \mu \text{AcM}^{-2} \) respectively, p<0-01).

**Discussion**

In these studies we have shown that inflamed mucosa but not quiescent mucosa from patients with ulcerative colitis releases PAF into culture medium. Furthermore, quiescent mucosa releases PAF when stimulated with bradykinin, 5-hydroxytryptamine, and co-cultured inflamed mucosa. Mucosa from normal, 'control' patients, however, did not produce any detectable PAF. Culture medium from any of the tissues will evoke an electrical response in stripped rat colon.

Inflamed tissue liberated PAF in greater quantities than previously reported, and this liberation was enhanced by exogenous bradykinin and 5-hydroxytryptamine. Therefore, it was not surprising to find that PAF release was attenuated by treatment with either darg arg leu bradykinin or ketanserin. The combined effect of these two antagonists was only sufficient to reduce PAF production by 50%. Presumably, other factors including those liberated by the enteric nervous and neuroendocrine systems are involved in PAF release. Although PAF was not detectable in quiescent mucosal cultures, its release was stimulated by exogenous bradykinin, 5-hydroxytryptamine, and coculture with colitic mucosa. These stimulants, however, did not influence control mucosa, unlike calcium ionophore and anti-human IgE, which have been shown to induce the release of PAF from normal control tissue as well as increase the production by inflamed tissue. Therefore, both control and quiescent tissue may be stimulated to liberate PAF but it
seems that under normal circumstances this membrane derived mediator is not produced in detectable amounts.

The PAF receptor antagonist did not influence PAF release by cultured mucosa. However, the phospholipase A2 inhibitors, mepacrine and hydrocortisone, significantly reduced the production of PAF and other phospholipid derivatives.\(^\text{14}\) Considering the wide range of immunomodulatory activities of steroids and the fact that mepacrine is only a phospholipase A2 inhibitor, it was surprising to find that mepacrine and hydrocortisone reduced the electrical response evoked by PAF.

Although PAF has been shown to stimulate intestinal section,\(^\text{13}\) the underlying mechanism remains unclear. We have shown that this effect is mediated by PAF receptors. Their activation has been shown to cause a rapid increase in intracellular calcium and hence secretion but this response was attenuated by cyclooxygenase inhibition.\(^\text{13}\) While both of these mechanisms may be important, their relevant contributions to PAF induced secretion were unknown. In this study combined inhibition of cyclooxygenase and lipoxygenase activity in rat colonic mucosa attenuated the PAF evoked secretory response by 70%. Furthermore, the maximum Isc response evoked by PAF occurred at the same concentration at which maximum eicosanoid release was stimulated \((10^{-5} \text{ M})\).\(^\text{14}\) Thus, these data suggest that eicosanoids, via their action on cAMP, are responsible for most of the PAF mediated secretory effect, while the remainder is likely to be related to changes in intracellular calcium.

In cultured colonic tissue, PAF stimulated a concentration dependent rise in both PGE\(_2\) and LTD\(_4\); similarly, PAF has been shown to augment the production of LT\(_B_4\) and 5 HETE.\(^\text{20-22}\) The threshold for a response in colonic tissue was in the range of \(10^{-8} \text{ M} \rightarrow 10^{-9} \text{ M}\), with a maximum stimulatory effect at a PAF concentration of \(10^{-5} \text{ M}\), considerably higher than the measured concentration \((828 (74) \text{ fmol})\) released by inflamed tissue. Thus, the quantity of PAF released by inflamed mucosa was much smaller than that required to produce even minimal secretory stimulation. Clearly, PAF is only one of the many mediators that are liberated during the inflammatory response and which will also drive secretion. It is likely that these mediators act together to drive secretion, hence smaller quantities of each mediator are required to achieve the same secretory effect. Furthermore, rapid activation of the phospholipases and acetyl hydrolases that catabolise PAF released from cultured colonic mucosa may contribute to the difference between the concentration of PAF released from cultured tissue and that required to stimulate secretion.

While PAF will stimulate the production of eicosanoids the underlying mechanism is unknown. Phospholipase A\(_2\) is required to release both types of membrane derived mediator, but it is unlikely to be implicated in this role as we have demonstrated that PAF attenuates rather than stimulates its own
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release. Although PAF may upregulate the activity of both cyclooxygenase and lipooxygenase, it seems likely that the PAF stimulated increase in both intracellular calcium and eicosanoid output is mediated by phospholipase C.

Although PAF stimulated eicosanoid release, these compounds did not account for all of its secretory action. Inhibition of phospholipase A2 derived secretagogues with either mepacrine or hydrocortisone reduced the culture medium evoked electrical response by approximately 81%, of which eicosanoids contributed nearly 60% and presumably PAF the remainder. There is, however, some disparity between this presumed secretory influence attributed to PAF (21%), and the actual response that it evoked (46%). Furthermore, medium from inflamed tissue treated with combined inhibition of cyclooxygenase, lipooxygenase, and PAF receptors attenuated the IC response by 69%, of which eicosanoids accounted for 58%. This disparity between the presumed and actual secretory response evoked by PAF indicates that much of this PAF response is mediated by eicosanoids. Although platelet activating factor and eicosanoids account for 69% of the secretory response evoked by culture medium, a further 12% is attributed to compounds that are antagonised by both mepacrine and hydrocortisone and it is likely that phospholipase C derivatives are involved. The residual medium evoked electrical response is presumably a reflection of a variety of cytokines and compounds released by the enteric nervous system.

It is interesting to speculate that as PAF accounted for, at most, 46% of the culture medium secretory effect, any therapeutic attempts to block PAF release/receptors in patients with ulcerative colitis will have a limited effect on their symptoms. Inhibition of one individual phospholipid derivative, or even one group of phospholipid derivatives is highly unlikely to produce any therapeutic benefit – as exemplified by the failure of non-steroidal anti-inflammatory drugs in the treatment of ulcerative colitis. In conclusion, we have shown not only that PAF stimulates colonic secretion, accounting for 46% of the secretory response evoked by culture medium from colitic tissue, but also that its actions are mediated, predominantly by eicosanoids.

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