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Partial purification and characterization of a formylmethionine deformylase from rat small intestine

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A formylmethionine deformylase from rat small-intestinal mucosa has been isolated, characterized and partially purified. The enzyme catalyses the release of equimolar amounts of formate and the free amino acid. The deformylase was active against formylmethionine (K_m 7.1 mM) and formylnorleucine, but showed reduced activity against formyl-leucine. It was inactive against a range of other polar and nonpolar formyl-amino acids and against formyl di- and tri-peptides. The M_r of the native enzyme was between 45000 and 66000, as determined by h.p.l.c. gel permeation. Further purification of the enzyme either by h.p.l.c. ion-exchange chromatography and concanavalin A–Sepharose or by isoelectric focusing yielded a preparation with one predominant band of M_r 50000 on SDS/polyacrylamide-gel electrophoresis. Bacteria in the intestine present the host with substantial amounts of formylmethionine (fMet) from proteinase and carboxypeptidase digestion of bacterial formyl-peptides in the intestinal lumen. fMet (0.01–1.0 mM) inhibited translation of a test RNA from brome mosaic virus *in vitro*, indicating that it could have adverse effects on cellular metabolism. Gut epithelial fMet deformylase may be required for deformylation of this exogenous (bacterial) and also endogenous (mitochondrial) fMet.

INTRODUCTION

Protein synthesis in bacteria (Dickerman & Smith, 1971; Marcker *et al.*, 1966), chloroplasts and mitochondria (Bianchetti *et al.*, 1971; Mahler *et al.*, 1972), is characterized by initiation through the addition of formylmethionine (fMet) as the *N*-terminal residue of nascent polypeptides. fMet is presented to the ribosome via the $tRNA_i$ (initiating tRNA) after donation of a formyl moiety from formyltetrahydrofolate to the Met-tRNA (Dickerman & Smith, 1971; Marcker *et al.*, 1966). In contrast, cytoplasmic eukaryotic protein synthesis utilizes only methionine in the initiation process. Furthermore, formylation of eukaryotic Met-$tRNA_i$ may have an inhibitory effect on protein translation (Brown & Smith, 1970; Caffier *et al.*, 1971).

In bacteria, deformylase enzymes have been described which are capable of cleaving the formyl residue either from formyl peptides, permitting post-translational processing from the *N*-terminal, or from free fMet (Adams, 1968). Nevertheless, deformylation in bacteria is incomplete, since *N*-formyl oligopeptides are found in bacterial culture supernatants (Schiffman *et al.*, 1975; Marasco *et al.*, 1984; Chadwick *et al.*, 1988) and have recently been demonstrated in fluid obtained from human large intestine by dialysis techniques *in vivo* (Chadwick *et al.*, 1988). These peptides are potent pro-inflammatory agents that induce cell adherence (Smith & Holers, 1980), chemotaxis (Ward *et al.*, 1968; Showell *et al.*, 1976), superoxide production (Simchowitz & Spilberg, 1979) and lysosomal enzyme secretion (Showell *et al.*, 1976) in mammalian neutrophil leucocytes, and tissue inflammation when introduced across normal epithelial barriers (Desai *et al.*, 1979; Jones *et al.*, 1977; Issekutz & Movat, 1980; Mellor *et al.*, 1986).

In the rat intestine we have previously shown that, at sites of bacterial colonization, both intra-luminal and mucosal proteinases and carboxypeptidases degrade pro-inflammatory *N*-formyl peptides (Woodhouse *et al.*, 1987). The metabolic fate of fMet residues is unknown. fMet might inhibit normal protein synthesis in the intestinal cells (Caffier *et al.*, 1971) and a deformylase enzyme would function to protect against intracellular accumulation of exogenous fMet from bacteria and possibly endogenous fMet from mitochondrial metabolism.

In this paper we describe the isolation, characterization and partial purification of a deformylase enzyme from rat intestinal epithelial cells and studies of the effect of fMet on translation of RNA in a eukaryotic system *in vitro*.

MATERIALS AND METHODS

Purification of deformylase

The distal 50% of the small intestines from six conventional male Wistar rats (Otago stock colony) and four germ-free rats (Walter & Elisa Hall Institute, Melbourne, Australia) were removed and flushed with 10 mM-sodium phosphate/0.5 M-NaCl, pH 7.5 (4 °C), to remove faecal material. The intestines were cut longitudinally and the mucosal surfaces were scraped in ice-cold 20 mM-sodium phosphate buffer, pH 7.4, (approx. vol. 150 ml). The mucosal scrapings were sonicated (5 × 10 s pulses, Branson Sonifier, microtip, output 6) on ice and mucus aggregates, cellular debris and brush-border-membrane vesicles were removed by centrifuging at 27000 *g* for 60 min at 4 °C.

Purification of the enzyme from the 27000 *g* super-

Abbreviations used: PAGE, polyacrylamide-gel electrophoresis; BMV, brome mosaic virus; DMSO, dimethyl sulphoxide.

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natant derived from normal rat ileum was performed as follows. The supernatant fraction was adjusted to pH 5.5 with diluted (1:5, v/v) glacial acetic acid at 2–4 °C. The precipitated material was removed by centrifugation (10000 *g* for 10 min at 4 °C).

The supernatant containing the deformylase activity was diluted to 200 ml with ice-cold distilled water and loaded on to a CM-Sephadex column (5 cm × 16 cm) pre-equilibrated to the Na^+ form at 4 °C. The column was washed batchwise at 200 ml/h with 200 ml volumes of buffer (50 mM-sodium acetate pH 5.5), increasing the NaCl content by 50 mM increments with each wash. The deformylase activity eluted from the cation exchanger at 50–150 mM-NaCl.

The active fraction was concentrated by ultrafiltration (Amicon cell, 90 lbf/in^2, 10000 molecular mass cut-off filters) to 12 ml and further purified by Sephadex G200 chromatography (60 cm × 2 cm, 0.1 M-sodium phosphate buffer, pH 7.5, 10 ml/h per fraction). The fractions (11–16) containing the activity were pooled, concentrated by ultrafiltration and rechromatographed by h.p.l.c. gel filtration using Waters Protein Pak 125 (7.8 mm × 30 cm) and Protein Pak 300 sw (7.5 mm × 30 cm) columns in series (0.5 ml/min, 0.1 M-sodium acetate, 0.25 M-NaCl, pH 6.0). The columns were calibrated using bovine serum albumin (66 kDa) and ovalbumin (45 kDa) as molecular-mass markers. The sample was injected in 1 ml aliquots and the fractions (1 min) were collected on ice. The injections were repeated until all the material had been fractionated and the fractions were collected repeatedly into the same tubes. The deformylase activity eluted from the gel columns in fractions 34–41. These fractions were pooled and dialysed overnight against 3 litres of 5 mM-phosphate buffer, pH 8.0, at 4 °C.

The enzyme was then further fractionated by h.p.l.c. anion-exchange chromatography using Waters ACCELL (quaternary methylamine) packed in a 40 cm × 4.5 mm (internal dimensions) stainless-steel column. The column was equilibrated in the Na^+ form, buffer B consisting of 20 mM-Tris/HCl (pH 8.0)/0.5 M-NaCl and buffer A, the same, but without NaCl. The gradient was delivered using two Waters h.p.l.c. pumps (model 510) operated through the Waters model 721 programmable system controller. The flow rate was 3 ml/min, except during re-equilibration when it was 5 ml/min. The gradient was: 0–6 min, 100% buffer A; 6–25 min, linear slope from 100% buffer A to 44% A; 25–27 min, linear slope 44% A to 0% A (i.e. 100% buffer B); and from 27–37 min, a wash of 100% buffer B. The sample was loaded by repeated injections (2 ml) and the gradient commenced after loading the entire preparation. Fractions were collected on ice and the deformylase activity eluted in fractions 14–18.

The pooled active fractions, diluted to 40 ml with 75 mM-sodium acetate/HCl buffer, pH 6.0, containing 1.0 mM-NaCl, 1.0 mM-$MgCl_2$ and 1 mM-$CaCl_2$, were then passed through a 1 cm × 15 cm glass column containing 5 ml of concanavalin A–Sepharose (Sigma). The deformylase activity was eluted in the void wash from this column. The deformylase preparation was concentrated using the Amicon Centricon 10 microconcentrator.

Assay for deformylase

Routinely, deformylase activity was monitored by fluorometric determination of the appearance of free methionine. In some cases the appearance of formate was determined as described by Makar *et al.* (1975). A typical assay contained 130 μl of 200 mM-sodium phosphate buffer, pH 8.0, 20 μl of 100 mM-fMet, and, after equilibration to 37 °C, 50 μl of enzyme. Aliquots of the reaction mixture were removed at suitable intervals and the reaction terminated by addition of an equal volume of ice-cold borate/0.81 M-KOH buffer, pH 10.6, containing 0.05% 2-mercaptoethanol. After generation of samples for methionine determination, the free amino acid was derivatized using an equal volume of *o*-phthalaldehyde (Serva) solution (15 mg of *o*-phthalaldehyde in 300 μl of methanol and 2.7 ml of borate/KOH buffer, containing 60 μl of 2-mercaptoethanol). After 1 min the samples were injected on to a 10 cm × 4.5 mm (internal dimension) lichroprep C_{18} column, using a Waters WISP automated injector. The running buffer was 53% (v/v) methanol in 10 mM-phosphate buffer, pH 7.5, delivered at 2.5 ml/min using an LKB h.p.l.c. pump. The fluorescent products were detected using a Waters 420E fluorescence detector (excitation at 325 nm, emission at 425 nm) and the peaks were integrated using a Waters Data Module.

Investigation of deformylase activity against formyl di- and tri-peptides was performed by reverse-phase chromatography of the reaction mixtures, looking for quantitative disappearance and shift in retention time of the product from the original parent peptide. The peptides were dissolved in 50 μl of dimethyl sulphoxide (DMSO) and diluted with 50 mM-Tris/HCl, pH 8.3, containing 0.02% (v/v) Tween 80. The chromatographic system for formyl peptides has been previously described (Chadwick *et al.*, 1988). Protein was assayed using the Pierce BCA protein method with bovine serum albumin (Sigma) as standard (Smith *et al.*, 1985).

SDS/PAGE

SDS/polyacrylamide-gel electrophoresis (PAGE) was by the procedure of Laemmli (1970) and the mini-gel apparatus described by Matsudaira & Burgess (1978). The separating gel was a 7–15% (w/v) acrylamide gradient and the stacking gel was 3.5% (w/v) acrylamide. Samples were diluted to the required concentration in sample buffer, which contained 3% (w/v) SDS, 8 M-urea, 70 mM-dithiothreitol, 1% Bromophenol Blue and 25 mM-Tris/HCl, pH 6.8. Samples were heated to 70 °C for 4 min before electrophoresis.

Isoelectric focusing

Isoelectric focusing was performed using an LKB2217 ultraphase apparatus and 0.5 mM-thick acrylamide slab gels (total acrylamide = 5%; cross-linker = 3.5%). The carrier ampholines were of pH range 4.0–6.5 and the electrode solutions (0.5 M) were acetic acid and NaOH. Focusing was performed at 1300 V for 90 min (10 °C). The gel was then sliced into 1.5 mm pieces and each slice incubated for 3 h (37 °C) in 200 μl of 0.2 M-phosphate buffer (pH 8.0) containing 10 mM-fMet. Deformylase activity was located using the formate assay. Supernatants from the active fractions were concentrated and dialysed using Amicon microconcentrations and subjected to SDS/PAGE.

Production of formyl amino acids

Amino acids were formylated according to the method of Sheehan & Yang (1958). The formyl derivatives were recrystallized as described and were suitable as

deformylase substrates after titration to neutral pH. For the translations *in vitro*, fMet was further purified by extraction into ethyl acetate at pH 1 in 0.1 M-HCl. The organic phase was freeze-dried and the extraction from aqueous to organic phase repeated 3 times. The product was finally freeze-dried and kept desiccated. For the production of acetyl and propionyl derivatives of methionine, the method of Sheehan & Yang (1958) was used with acetic or propionic acids replacing formic acid.

Translations of RNA *in vitro*

Brome mosaic virus (BMV) RNAs 1 and 2 (Amersham) were translated essentially as described by Pelham & Jackson (1976), by using reticulocyte lysate obtained from Amersham. Each incubation contained 7 μl of reticulocyte lysate, 1 μl of BMV RNA (0.5 μg), 3.5 μCi (1 μl) of [^{35}S]methionine (1100 Ci/mM) (Amersham) or 0.5 μCi (1 μl) of U-^{14}C-labelled amino acid mixture (minus methionine or histidine; Amersham, CFB.152, 10 mCi/mmol) and 1 μl of fMet or Milli Q water. After incubation for 1 h at 30 °C, 2 μl of each reaction mixture was spotted on to Whatman no. 1 paper and successively placed in ice cold 10% (w/v) trichloroacetic acid for 10 min, transferred to hot (90 °C) 5% (w/v) trichloroacetic acid for a further 10 min, and then soaked in ethanol/ether (50:50, v/v) before drying under a heat lamp. The radioactivity was determined by scintillation counting using Triton X-100 /toluene scintillation fluid. The remaining translation products were solubilized in an equal volume of SDS/PAGE sample buffer and fractionated by electrophoresis. The gels were fixed (10 min) in 20% (v/v) propan-2-ol, 10% (v/v) acetic acid, and then transferred to DMSO for 1 h. The DMSO was then replaced and after a further 1 h the gel was transferred to 100 ml of DMSO containing 20 g of naphthalene and 0.5 g of 2,5-diphenyloxazole. After 45 min the gel was washed in running tap water for at least 2 h. The gel was dried (LKB gel drier) and placed against Kodak XRP-1 X-ray film for the desired time period.

RESULTS

Source of fMet deformylase activity

fMet deformylase was isolated from normal and germ-free animals. The specific activity of the enzyme was similar in homogenates of ileal mucosal tissue obtained from four conventional (0.080 ± 0.018 μmol $\cdot$ min^{-1} $\cdot$ mg of protein^{-1}) and four germ-free rats (0.054 ± 0.013 μmol $\cdot$ min^{-1} $\cdot$ mg of protein^{-1}). This confirmed that the enzyme was derived from the host rather than contaminating bacteria.

Purification

Table 1 details the purification and recovery of fMet deformylase from rat ileal mucosa. The deformylase activity remained soluble after centrifugation to remove organelles and brush-border-membrane vesicles. Fractionation of the activity on h.p.l.c. gel filtration indicated that the enzyme had a native M_r between 66000 and 45000. Concanavalin A–Sepharose chromatography indicated that the enzyme was not a 'simple' glycoprotein; however, this step removed contaminating glycoproteins from the preparation. SDS/PAGE demonstrated that the purified enzyme (final purification 1913-fold) contained one major band of M_r-50000, with a number of weakly staining bands also evident (Fig. 1, lane 3). The 50000 band was also demonstrated after recovery of the enzyme activity from an isoelectric-focusing gel (enzyme pI 5.2–5.5), indicating that the enzyme was associated with this band (Fig. 1, lane 4).

Table 1. Purification of deformylase activity from rat ileum

Purification step	Specific activity (μmol/min per mg of protein)	Purification (-fold)	Recovery (%)
Crude preparation	0.07	1	100
Centrifugation (27000 *g*)	0.21	3	96
Acidification	0.35	5	95
CM-Sephadex	1.36	20	70
Sephadex G200	4.22	60	66
H.p.l.c. (gel-filtration)	7.94	113	47
H.p.l.c. (anion-exchange)	48.80	697	22
Concanavalin A–Sepharose	133.96	1913	21

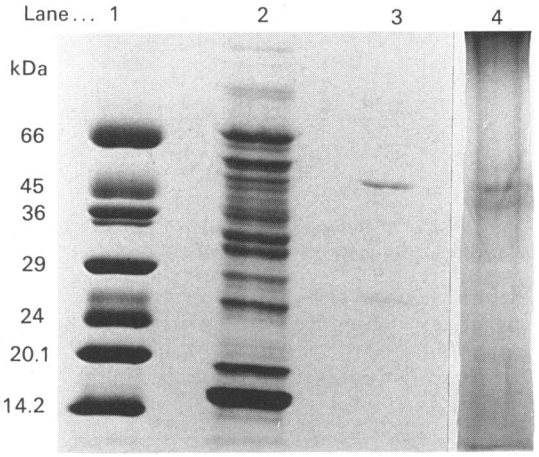

Fig. 1. SDS/PAGE of fMet deformylase

Electrophoresis was performed using a 9–15% (w/v) acrylamide-gradient gel and the Laemmli (1970) buffer system. Lanes are: lane 1, molecular-mass standards; lane 2, 27000 *g* original supernatant; lane 3, purified deformylase preparation after ion-exchange and concanavalin A–Sepharose chromatography showing major band at M_r 50000; lane 4, purified deformylase preparation after isoelectric focusing showing major band at M_r 50000. Proteins in lanes 1–3 were detected by Coomassie Blue staining and in lane 4 by the silver stain method of Adair *et al.* (1982). The molecular-mass markers were: bovine serum albumin, 66 kDa; ovalbumin, 45 kDa; glyceraldehyde-3-phosphate dehydrogenase, 36 kDa; carbonic anhydrase, 29 kDa; trypsinogen, 24 kDa; trypsin inhibitor, 20.1 kDa; lactalbumin, 14.2 kDa.

Biochemical characterization

Deformylation of fMet resulted in equimolar release of the parent amino acid and formate over a 60 min incubation period. Optimal deformylase activity was observed at pH 8–9, with catalysis being strongly inhibited below pH 6.0 (Fig. 2*a*). Maximal reaction rate was observed at 55 °C over a 10 min incubation period;

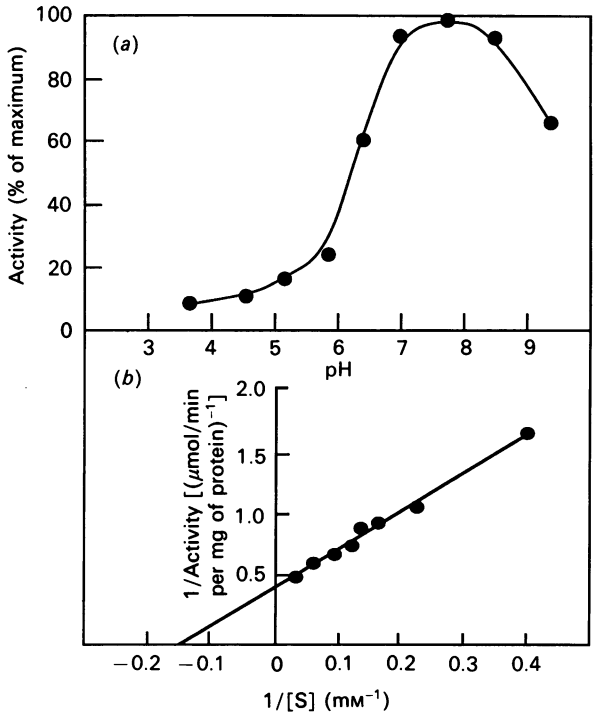

Fig. 2. pH profile of deformylase activity (*a*) and Lineweaver–Burk plot for deformylase activity against fMet

(*a*) Deformylase was assayed as described in the Materials and methods in 0.2 M-phosphate buffers. The most alkaline buffer was obtained by addition of 0.1 M-sodium carbonate. (*b*) Deformylase was assayed as described in the Materials and methods.

however, after a 1 h incubation of the enzyme at 55 °C there was a 42% loss of catalytic activity. The k_m for the enzyme with fMet as substrate was 7.1 mM as determined from the Lineweaver–Burk plot of 1/velocity versus 1/[substrate] (Fig. 2*b*). Deformylase activity was found to be unaffected by the addition of azide (5 mM), phenylmethanesulphonyl fluoride (0.5 mM), EDTA (50 mM), or benzyl succinate (25 mM) (an inhibitor of metallocarboxypeptidases; Cushman & Ondetti, 1981). The enzyme was however strongly inhibited by the addition of 20 mM-dithiothreitol (86%) and 10 mM-iodoacetamide (80%).

The enzyme was tested for activity against a range of polar and non-polar formyl amino acids. The enzyme was most active against formylnorleucine and fMet, and showed reduced activity against formyl-leucine and no activity against formyl derivatives of isoleucine, phenylalanine, valine, glutamic acid, serine, alanine and arginine. The enzyme was also inactive against fMet-Phe, fMet-Val, fMet-Trp, fMet-Met-Met, fMet-Ala-Gly-Ser-Glu, fMet-Leu-Phe and fMet-Leu-Tyr.

To investigate further the substrate specificity of the deformylase activity, acetyl and propionyl derivatives of methionine were synthesized. Both analogues of fMet were hydrolysed at a reduced rate compared with the biological substrate. For example, an aliquot of deformylase which hydrolysed 8.9 nmol of fMet/min at 37 °C only hydrolysed 2.6 nmol of either substrate analogue under the same conditions. Although the substrate analogues were catalysed with a reduced $V_{max.}$, both exhibited lower K_m values compared with fMet, being 0.22 mM for acetyl-Met (Fig. 3*a*) and 0.33 mM for propionyl-Met (Fig. 3*c*). Furthermore, both substrate analogues inhibited hydrolysis of fMet in a competitive fashion; the K_i for acetyl-Met inhibition was 0.16 mM (Fig. 3*b*) and for propionyl-Met was 0.17 mM (Fig. 3*d*).

Effect of fMet on eukaryotic translation

The effect of fMet on translation *in vitro* of BMV RNA are shown in Fig. 4*a*. Lane 1 shows, in the absence of fMet, the two [^{35}S]methionine-labelled polypeptide products of the translation system. Lanes 2–4 show the effects of increasing concentrations of fMet on [^{35}S]Met incorporation (lane 2, 20 μm; lane 3, 100 μM and lane 4, 1.0 mM). fMet added at 100 μM almost totally inhibited incorporation of radioactivity into translation products, and some inhibition was also evident at 10 μM.

The reticulocyte lysate preparation contained no intrinsic deformylase activity, which would generate methionine from added fMet and thereby reduce the specific radioactivity of the [^{35}S]Met for the labelling of translation products. Following incubation (2 h) of reticulocyte lysate with 1.0 mM-fMet, no free methionine was detected (sensitivity of assay 5 pmol). Secondly, 10 nmol of fMet was analysed and shown to contain Ser (22 pmol), Gly (15 pmol), Tyr (10 pmol), but no free Met. Moreover, translation of the BMV RNA using ^{14}C-labelled amino acid mixtures devoid of added methionine was also inhibited by 1 mM-fMet (Fig. 4*b*, lane 4).

DISCUSSION

This study has confirmed the presence of a fMet deformylase enzyme in the ileal mucosa of the rat. The enzyme was a polypeptide of M_r 50000 present in the 27000 *g* supernatant of the mucosal extract. Substrate specificity studies confirmed activity against fMet and formylnorleucine, reduced activity against formyl-leucine and no activity against other formyl amino acids, formyl di- or tri-peptides.

This specificity suggests a role for the enzyme in the deacylation of fMet residues generated by peptidase action on signal peptides with formylmethionyl *N*-termini. In eukaryotes the only endogenous source of such peptides is mitochondrial protein biosynthesis (Mahler *et al.*, 1972), whereas fMet initiation is the rule in prokaryotes (Dickerman & Smith, 1971; Marcker *et al.*, 1966). The enzyme might thus serve a dual function by preventing intracellular accumulation of both endogenous (mitochondrial) and exogenous (bacterial) fMet. Intestinal epithelial cells are exposed to the products of bacterial metabolism in the gut lumen and such a role for the enzyme is especially appropriate at this site.

The enzyme did not show absolute specificity for the formyl acyl group, since acetyl- and propionyl-Met were both cleaved, although at reduced reaction rates compared with fMet. The K_m for acetyl- and proprionyl-Met were lower (0.22 mM and 0.3 mM, respectively) than for fMet (7.1 mM) and both of these analogues were competitive inhibitors of fMet deformylation. This suggested that the binding affinity of the substrate for the enzyme active site was influenced by the nature of the acyl group, but that catalysis was favoured in the presence of a formyl group. Both binding affinity and catalysis were clearly also highly dependent on their amino acid *R*

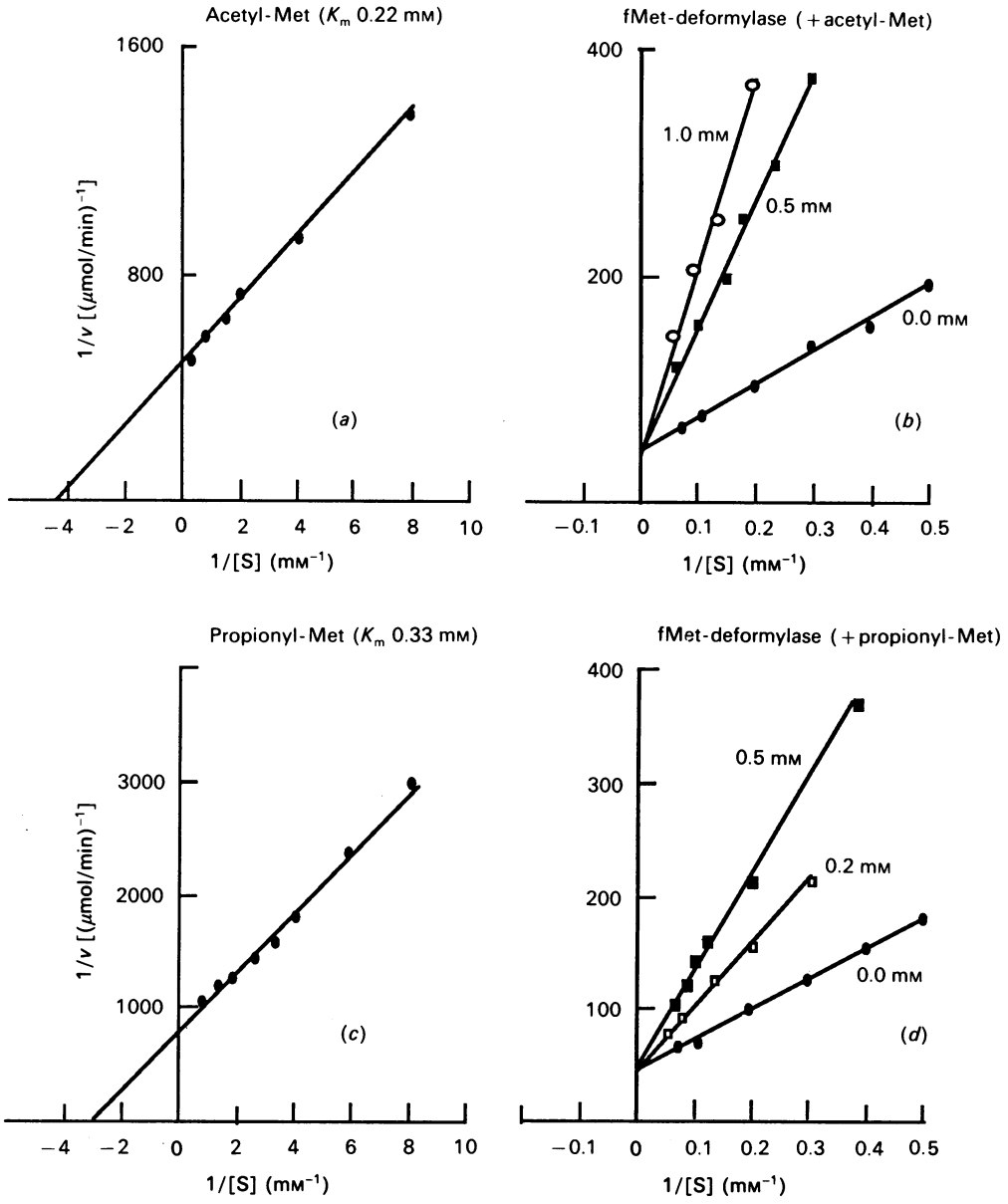

Fig. 3. Lineweaver–Burk plot for the hydrolysis of acetylmethionine by deformylase (*a*), for the inhibitory effect of acetylmethionine on fMet deformylase (*b*), for the hydrolysis of propionylmethionine by deformylase (*c*), and for the inhibitory effect of propionylmethionine on fMet deformylase (*d*)

(*b*) (○), 1.0 mM-acetylmethionine; (■), 0.5 mM-acetylmethionine; (●) without acetylmethionine. (*d*) (■), 0.5 mM-propionylmethionine; (□), 0.2 mM-propionylmethionine; (●), without propionylmethionine.

group, methionine and norleucine possessing favourable side-chains and leucine apparently being sterically less well suited.

Deformylases have been described in extracts from *Escherichia coli* (Adams, 1968) and *Euglena gracilis* (Aronson & Lugay, 1969). Of greater relevance to this study, however, was the demonstration by Yoshida & Lin (1972) of an fMet deformylase in crude extracts of rabbit reticulocyte lysates. This enzyme cleaved the formyl moiety from fMet and formyl-leucine and acetyl groups from acetyl-Met, acetyl-Leu and acetyl-Val. The enzyme co-migrated with a dipeptidase activity on starch gels, but was not further characterized. The same extracts contained a formyl aminopeptidase which cleaved fMet from a number of formyl peptides and a similar fMet-releasing enzyme has been described in rat liver (Suda *et al.*, 1980).

The organ distribution of fMet deformylase was not investigated in detail in this study. However, deformylase activity was also present in rat colon, liver and kidney and in mucosal homogenates from human ileal and colonic biopsies, suggesting that the enzyme was not organ- or species-specific.

To investigate the effects of fMet on eukaryotic protein biosynthesis, we chose to study the translation *in vitro* of a test RNA (BMV RNA) using reticulocyte lysates.

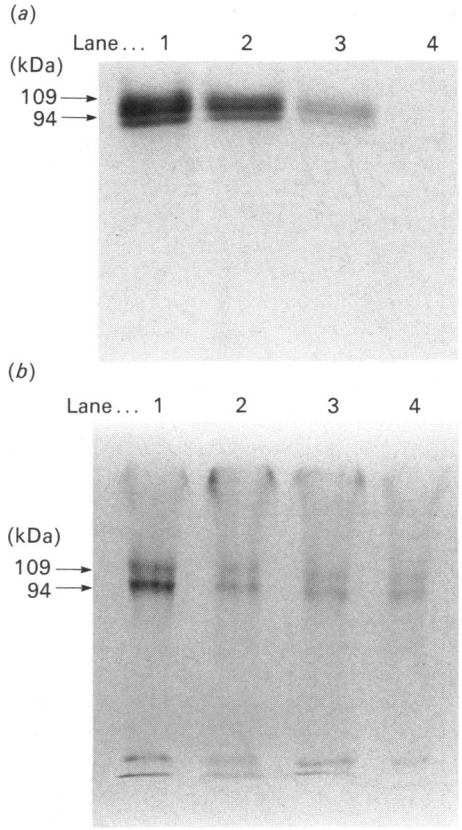

Fig. 4. The effects of fMet on translation *in vitro* of BMV RNA 1 and 2

The radiolabelled products of translation were fractionated by SDS/PAGE. (*a*) Translation using [^{35}S]methionine: lane 1, minus fMet; lane 2, 20 μM-fMet; lane 3, 100 μM-fMet; lane 4, 1 mM-fMet. (*b*) Translation using U-^{14}C-labelled amino acids: lane 1, minus fMet; lane 2, 20 μM-fMet; lane 3, 100 μM-fMet; lane 4, 1 mM-fMet.

Translation was inhibited by fMet concentrations > 10 μM. This effect was observed using both [^{35}S]Met and ^{14}C-labelled amino acids independent of methionine to label the translation products. There are two possible mechanisms for the inhibition. First, mammalian Met-tRNA synthetase is inhibited by fMet or secondly, Met-tRNA itself is charged with fMet instead of the free amino acid. These possibilities remain to be investigated using purified Met-tRNA synthetase. We have, however, demonstrated 63% inhibition of bacterial Met-tRNA synthetase activity by addition of fMet (Broom, M. F. & Chadwick, V. S., unpublished work).

The biological effects of formyl peptides and the metabolic fates of these pro-inflammatory compounds are of great interest. An intestinal mucosal deformylase may represent one mechanism in mammalian metabolism for processing and thus protecting against potentially harmful bacterial products present in the gastrointestinal tract.

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