Glutamine metabolism in the gastrointestinal tract of the rat assessed by the relative activities of glutaminase (*EC* 3.5.1.2) and glutamine synthetase (*EC* 6.3.1.2)

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(*Received 3 July 1997 – Revised 10 October 1997 – Accepted 13 October 1997*)

The activities of the two key enzymes involved in glutamine metabolism, glutaminase (*EC* 3.5.1.2) and glutamine synthetase (*EC* 6.3.1.2), have been measured in the various tissues of the gastrointestinal (GI) tract of the rat, from the mouth to the rectum. Glutaminase activity was particularly high in the mucosa of the small intestine, where its activity accounted for more than 80 % of the total activity of the GI tract. In contrast, the mouth and oesophagus had very low activities, accounting for less than 2 % of the total. Glutamine synthetase was mainly confined to the lower part of the stomach, which accounted for almost 90 % of the total activity of the GI tract. Activity in the small intestine was very low, accounting for less than 2 % of the total, and similarly low levels were found in the mouth and oesophagus. The data provide the most complete information on the distribution of these enzymes in the GI tract of the rat and suggest: (a) that the mucosa of the small intestine has the highest capacity for glutamine breakdown but the lowest capacity for its synthesis, and so requires an external source of this amino acid; (b) that there is little potential for glutamine synthesis or breakdown in the mouth and oesophagus; and (c) that the lower stomach has a substantial capacity to synthesize glutamine, in contrast to the rest of the GI tract. The results of the investigation are relevant to sites of glutamine metabolism in therapeutic studies involving glutamine administration discussed with reference to reports of the effects of glutamine administration on GI tract injury.

Gastrointestinal tract: Glutaminase: Glutamine synthetase: Rat

With its multiple biochemical functions and high rate of inter-organ flux, glutamine has long been recognized as a particularly important amino acid (Krebs, 1980; Elia, 1991, 1996). The recent suggestion that in certain disease states, e.g. trauma, sepsis, burns, major surgery and uncontrolled diabetes, the availability of glutamine from endogenous tissue production may not be sufficient to maintain optimal tissue structure and function, has led to its reclassification as a 'conditionally essential' amino-acid (Lacey & Wilmore, 1990; Elia, 1992).

The mucosa of the gastrointestinal (GI) tract is a major site of glutamine utilization (Elia, 1996). Glutamine is a preferred energy source for the rapidly dividing enterocytes of the small and large intestines and is essential for maintaining normal integrity, structure and function of the mucosa. Additionally, its administration, often in substantial amounts, has been found to have a beneficial trophic effect on mucosal structure (Wusteman *et al.* 1995) and function and to reduce morbidity and mortality associated with severe enteropathies. In animals, glutamine administration attenuates intestinal atrophy associated with parenteral nutrition (Yoshida *et al.* 1992), increases splanchnic blood flow (Houdijk *et al.* 1994) and improves recovery from enterocolitis due to radiation or cytotoxic drug administration (Fox *et al.* 1988; O'Dwyer *et al.* 1989; Klimberg *et al.* 1990). Results from human studies are less conclusive. Administration of glutamine (or glutamine dipeptides) to post-operative patients has been reported to improve N balance (Souba *et al.* 1990) and, in those subjected to mucosa-damaging aggressive chemotherapy, to reduce infections and shorten the length of hospital stay (Schloerb & Amare, 1991; Ziegler *et al.* 1992). However, glutamine therapy was without effect on oral or oesophageal mucositis resulting from the use of cytotoxic drugs (Jebb *et al.* 1994, 1995). Other reports suggest a role for glutamine in healing stomach ulcers (Shive *et al.* 1957) and

Abbreviations: GI, gastrointestinal.

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pouchitis (Wischemeyer *et al.* 1993) and a reduction in chemotherapy-induced fever and endotoxin translocation (Poynton *et al.* 1995).

Currently, glutamine is being administered to patients with a range of GI tract diseases even though there is a far from complete knowledge about the precise site of glutamine utilization, and the tissues most likely to benefit from this treatment. Although arterio–venous differences across the splanchnic tissues demonstrate that the GI tract as a whole has a high requirement for glutamine (Windmueller, 1982), there is little information about its utilization by different parts of the tract. One way of gaining this more specific information is to measure the activities of the key enzymes involved in glutamine catabolism (glutaminase; *EC* 3.5.1.2), and synthesis (glutamine synthetase; *EC* 6.3.1.2). A tissue with high synthetase activity and low glutaminase activity would suggest that the tissue is self-sufficient or even a net producer of glutamine, whereas a tissue with high glutaminase activity but low synthetase activity suggests dependency of the tissue on an external supply. Such information could be relevant to studies involving administration of glutamine to treat GI disorders.

Although several workers have measured the activities of glutaminase and glutamine synthetase in the GI tract of the rat (Lund, 1970; Pinkus & Windmueller, 1977; Arola *et al.* 1981*a*), the information is incomplete for several reasons. First, many studies have concentrated on measuring the activity of only one of the enzymes at a specific site in the GI tract, e.g. only glutamine synthetase in the duodenum (Lund, 1970), or in the stomach and intestine (Arola *et al.* 1981*a*). Second, a number of other studies have assessed enzyme activities in rats of different ages and stages of development (Arola *et al.* 1981*b*; Remesar *et al.* 1985; Hahn *et al.* 1988) or in different circumstances e.g. pregnancy (Remesar *et al.* 1982; Ardawi, 1987*a*), burn injury (Ardawi, 1988*a*), after dexamethasone administration (Ardawi *et al.* 1988; Fox *et al.* 1988), in diabetes (Watford *et al.* 1984; Ardawi, 1988*b*), sepsis (Ardawi *et al.* 1991) and starvation (Budohoski *et al.* 1982). Third, different studies have used different methods of tissue preparation and different assays to measure enzyme activities. Furthermore, there are no reports which address the following issues: the relative contributions of mucosal and non-mucosal layers; enzyme activities in the mouth and oesophagus, which can become severely inflamed following radiotherapy or chemotherapy; the quantitative distribution of total enzyme activities in various parts of the GI tract; or total glutaminase and glutamine synthetase activities in the GI tract relative to other organs of the body.

Therefore, the aims of the present study were to determine the distribution of glutaminase and glutamine synthetase throughout the GI tract of the rat, to evaluate kinetic parameters of glutaminase, and to relate tissue concentrations of glutamine and glutamate to the enzyme activities in the different tissues. Such knowledge will allow a more informed decision to be taken about the probable sites of glutamine metabolism in the GI tract and whether glutamine administration might be expected to produce beneficial effects.

Methods

Animals

Individually housed male rats, from the Dunn Nutrition Centre's colony of hooded rats, were maintained on a standard laboratory diet at 22° with a 12 h light–dark cycle and free access to food and water (unless otherwise stated). They were fed on standard rat chow pellets in which approximately 60 % of total energy was supplied by carbohydrate and 20 % each by fat and protein. Rats were used in the study when they were 40–47 d of age and weighed approximately 150–200 g. Food was not restricted before use.

Tissue preparation

Animals were killed by cervical dislocation and the whole of the GI tract was rapidly removed into ice-cold saline (9 g NaCl/l). The stomach was cut into two equal halves and both the small and large intestines were divided into three sections of equal length. The sections were washed by flushing ice-cold saline through the lumen and were freed of mesenteric fat. They were opened longitudinally, given a further rinse and then blotted to remove mucus. The mucosa of the stomach and intestinal sections was freed from underlying muscle by scraping with a microscope slide on an ice-cold glass surface. This was not possible for the mouth and oesophagus, so in these cases the whole tissue was used for enzyme analysis. All tissue preparations, both mucosal and non-mucosal were weighed, then homogenized (15 000 rev./min for 20–30 s) in 10 volumes of ice-cold extraction buffer (50 mM-Tris containing 2 mM-EDTA, pH 7·9), using an Omni 1000 homogenizer (Omni International, Waterbury, CT, USA). The homogenate preparations were used to measure glutaminase, which is attached to the inner wall of the mitochondria. For glutamine synthetase, which is a cytosolic enzyme, the homogenate was first centrifuged (2000 ***g*** for 10 min at 4°) to give a clear supernatant fraction.

Enzyme assays

Glutaminase. The activity of this enzyme was measured in two ways, a radiochemical technique based on the method of Fox *et al.* (1988) and a spectrophotometric assay. For the radiochemical assay, a portion of each homogenate was further diluted tenfold with extraction buffer and 50 µl of the suspension was incubated with L-[U-^{14}C]glutamine, 1·85 KBq (2960 MBq/mmol) + 4 mM-unlabelled glutamine, 1·0 mM-potassium cyanide, 8·0 mM-imidazole and 150 mM-potassium phosphate buffer at pH 8·2, in a total volume of 0·25 ml.

After incubation for 30 min at 37°, the reaction was terminated by addition of 1 ml ice-cold 20 mM-imidazole-HCl buffer, pH 7·5. Samples were centrifuged at 2000 ***g*** for 5 min and 1 ml supernatant fraction was loaded on to a 4 ml column of AG-1X8 anion exchange resin (200–400 mesh, chloride form; Bio-Rad, Hemel Hempstead, Herts., UK) which had been equilibrated with 20 mM-imidazole-HCl buffer, pH 7·5. The column was washed sequentially with

7 ml imidazole buffer, then 1 ml 0·1 M-HCl. Glutamate was eluted by addition of a further 3 ml 0·1M-HCl and a 0·5 ml portion was taken for quantitation of ^{14}C in a liquid scintillation counter. Incubations were performed in duplicate and two portions from each were counted. Blanks lacking the homogenate were included in each assay.

The spectrophotometric assay was used in the determination of the kinetic parameters of the enzyme in high-activity intestinal mucosal preparations. The preparation, dilution and incubation of the tissue extract were as described for the radiochemical assay except that no labelled glutamine was used. The incubation was terminated by addition of 0·5 ml 5-sulfosalicylic acid (30 g/l). Samples were centrifuged at 2000 *g* for 5 min and glutamate concentration measured on the un-neutralized supernatant fraction by the method of Lund (1974).

Preliminary work showed that results obtained by these two methods were virtually identical. The radiochemical method was particularly useful for samples with low glutaminase activity, due to its greater sensitivity.

Glutamine synthetase. This enzyme was measured by a modification of the method of King *et al.* (1983). A portion of each homogenate was centrifuged, 2000 *g* for 10 min at 4°. A 20 µl sample of the supernatant fraction was added to 180 µl reaction mixture which contained L-[U-^{14}C]glutamic acid, 9·25 KBq (740 MBq/mmol) plus 20 mM-unlabelled glutamic acid, 20 mM-$MgCl_2$, 20 mM-NH_4Cl, 15 mM-ATP, 10 mM-phosphocreatine, 1·2 units creatine kinase (*EC* 2.7.3.2) and 50 mM-imidazole-HCl buffer, pH 7·6. Following incubation at 37° for 45 min, the reaction was terminated by addition of 1 ml ice-cold 20 mM-imidazole-HCl buffer, pH 7·5, and after mixing, 1 ml of the incubate was loaded on to a 4 ml column of AG-1X8 anion exchange resin, prepared as described for the glutaminase assay. Imidazole-HCl buffer (20 mM, 5 ml) was added to the column and the entire effluent collected. After mixing, a portion (1·5 ml) was counted in a liquid scintillation counter. Assays were performed in duplicate, and two portions from each assay were counted. Incubated blanks contained tissue extract but were without ATP.

Determination of tissue glutamine and glutamate concentrations. Blood was collected by cardiac puncture into heparinized tubes and plasma was prepared by centrifugation at 5 000 *g* for 5 min. Samples were deproteinized with 2 volumes of sulfosalicylic acid (30 g/l). Tissue samples were obtained as described for the enzyme assays but were then homogenized in 2 volumes of sulfosalicylic acid (30 g/l). Protein-free extracts of plasma and tissue were obtained by centrifugation, 5 000 *g* for 10 min. Glutamine and glutamate in the supernatant fraction were assayed enzymically by the method of Lund (1974).

Protein was measured by a Coomassie Blue technique (Pierce & Warriner UK Ltd, Chester, Ches., UK), after it had been solubilized with 0·2 M-NaOH.

Results

The distribution pattern of enzyme activities was the same irrespective of whether results were expressed in relation to wet weight of tissue or protein content. Glutaminase activity was generally higher in the mucosal tissues than in the non-mucosal layers (Fig. 1). The mucosa of the small intestine had by far the highest level of activity of this enzyme, reaching 169 nmol glutamate formed/min per mg protein in the proximal region of the small intestine which included the duodenum. The next highest tissue was mucosa from the distal small intestine, essentially the ileum, and then from the central, mainly jejunum, region. Mucosa from the colon had far less glutaminase activity and this diminished as one progressed down the organ. Activity in the stomach mucosa was low and did not differ from the values observed in the non-mucosal tissue from this organ. Other non-mucosal tissues including the mouth and oesophagus all had low levels of glutaminase activity in the range 20–41 nmol glutamate formed/min per mg

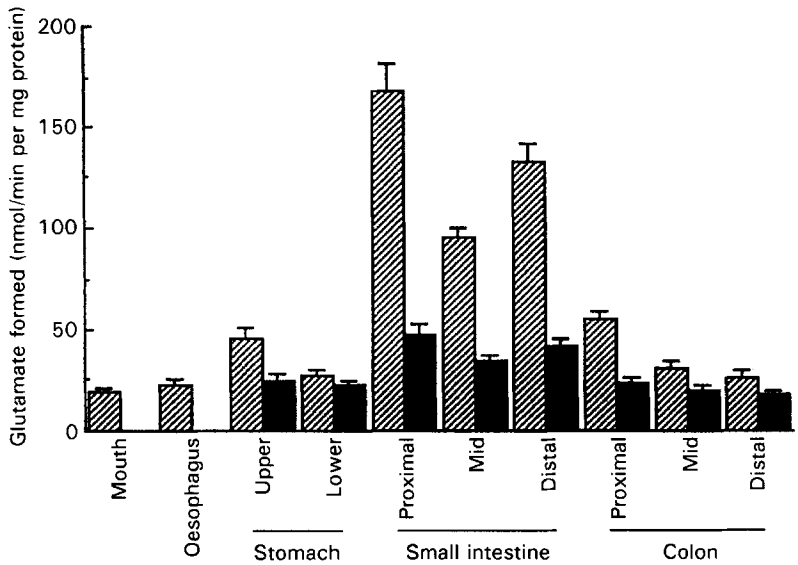

Fig. 1. Specific activity of glutaminase (nmol glutamate formed/min per mg protein) in mucosal (▨) and non-mucosal (■) tissues of the gastrointestinal tract of rats. Values are means for seven rats, with their standard errors represented by vertical bars.

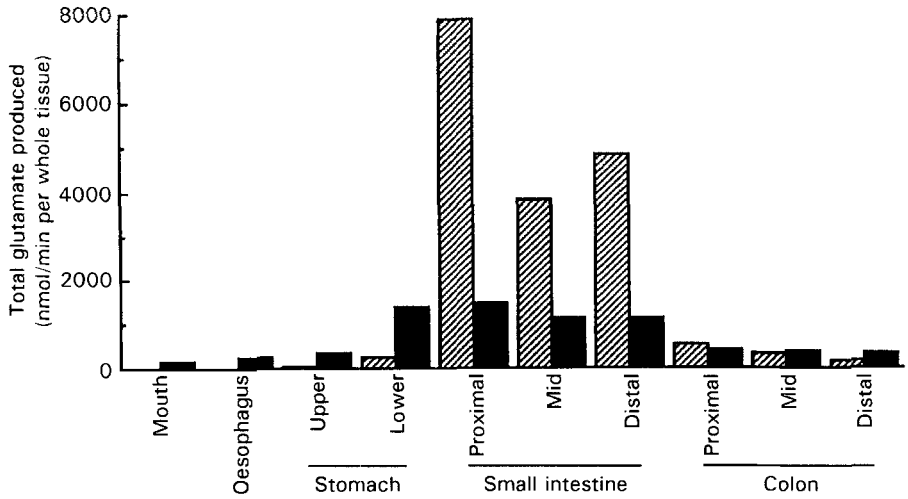

Fig. 2. Total glutaminase activity in mucosal (▨) and non-mucosal (■) tissues throughout the gastrointestinal tract of the rat. Tissue weights used in the calculations were as shown in Table 1. Values are means for seven animals.

protein. The highest non-mucosal values were found in the small intestine but these may have been due to some enterocytes remaining on the scraped tissue.

Fig. 2 shows the mucosal and non-mucosal distribution of total glutaminase activity from the mouth to the rectum calculated using the tissue weights shown in Table 1. It emphasizes the fact that more than 80% of all glutaminase activity in the GI tract is in the small intestine and most of it in the mucosa. The large intestine accounts for 8·4% of the total activity and the mouth, oesophagus and stomach combined, for only 8·1% . Total measured activity was about 24 μmol glutamine hydrolysed per min for the whole GI tract.

The distribution of glutamine synthetase activity in the GI tract was quite different (Fig. 3). The activity of this enzyme was extremely low in both the mucosal and non-mucosal tissue of the small intestine, being less than 0·4 nmol glutamine synthesized/min per mg protein. Similarly low values were obtained in the mouth and oesophagus. The colonic mucosa had rather higher activity, but both mucosal and non-mucosal tissue from the lower half of the stomach demonstrated by far the greatest activity, reaching rates of 35·4 and 34·2 nmol glutamine produced/min per mg protein respectively.

When expressed as total activity (Fig. 4), it is clear that only the lower part of the stomach (mainly the non-mucosal layer) has a significant capacity to synthesize glutamine, and this region accounted for almost 90% of the total 2·5 μmol glutamine synthesized per min in the GI tract.

Kinetic parameters of phosphate-dependent glutaminase

The concentration of glutamine in the incubation mix was varied over the range 2–20 mM. Typical Michaelis saturation curves were obtained for glutaminase from both small intestinal and colonic mucosas. However, a double reciprocal plot of enzyme activity (V) *v.* substrate concentrations was not always found to be linear. Since the double reciprocal plot emphasizes the points at low substrate concentration (which are the least accurate), the kinetic parameters were evaluated by a simple least-square fitting of the untransformed data to a rectangular hyperbola described by the equation $V = V_{max} \times S/(K_m + S)$. Table 2

Table 1. Tissue weights (per 100 g body weight) throughout the gastrointestinal tract of rats (mean body weight 175 g)
(Mean values and standard deviations for fourteen rats)

	Weight			Weight			Weight	
Tissue	Mean	SD	Tissue	Mean	SD	Tissue	Mean	SD
Mouth	0·20	0·04	Small intestine			Large intestine		
Oesophagus	0·17	0·04	Proximal:			Proximal:		
			mucosa	0·46	0·09	mucosa	0·11	0·05
Stomach			non-mucosa	0·32	0·06	non-mucosa	0·20	0·06
Upper:			Mid:			Mid:		
mucosa	0·03	0·02	mucosa	0·38	0·09	mucosa	0·10	0·05
non-mucosa	0·20	0·03	non-mucosa	0·36	0·08	non-mucosa	0·25	0·05
Lower:			Distal:			Distal:		
mucosa	0·13	0·09	mucosa	0·36	0·07	mucosa	0·07	0·06
non-mucosa	0·60	0·07	non-mucosa	0·32	0·06	non-mucosa	0·21	0·08

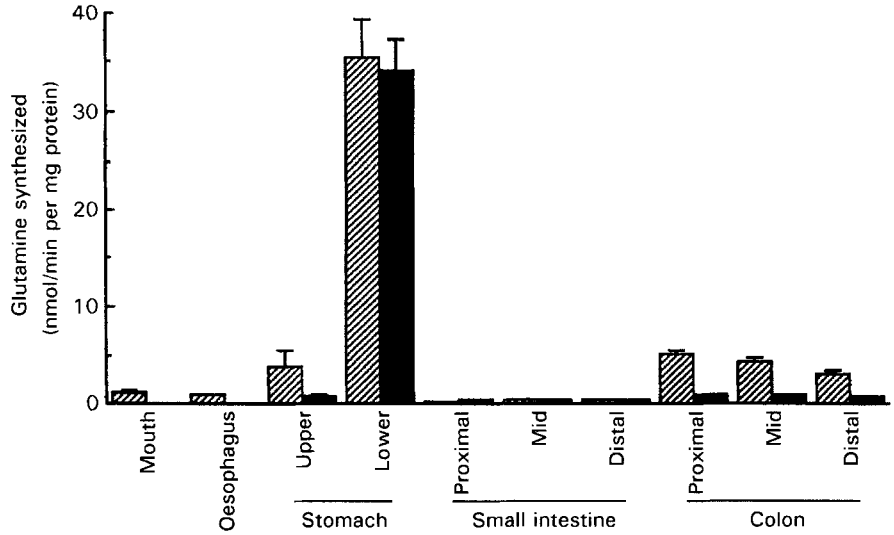

Fig. 3. Specific activity of glutamine synthetase (nmol glutamine formed/min per mg protein in mucosal (▨) and non-mucosal (■) tissues of the gastrointestinal tract of the rat. Values are means for seven rats, with their standard errors represented by vertical bars.

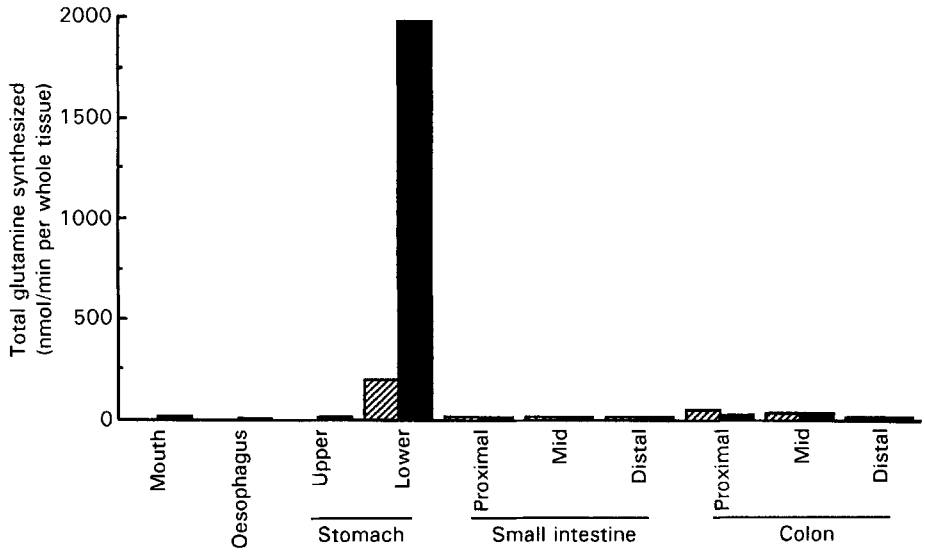

Fig. 4. Total glutamine synthetase activity in mucosal (▨) and non-mucosal (■) tissues throughout the gastrointestinal tract of the rat. Tissue weights used in the calculations were as shown in Table 1. Values are means for seven animals.

Table 2. Kinetic parameters of phosphate-dependent glutaminase from the small and large intestinal mucosa of the rat

(Mean values and standard deviations)

		Glutaminase activity			
		V_{max} (μmol glutamate formed/min per g wet wt)		K_m (mM)	
Tissue	*n*	Mean	SD	Mean	SD
Small intestine	7	24·9	6·5	2·67	0·2
Large intestine	5	8·9***	1·7	1·69***	0·3

Mean values were significantly different from those for the small intestine, ***$P < 0.001$.

gives values for maximum velocity (V_{max}) and Michaelis constant (K_m). Both V_{max} and K_m were higher in the mucosa from the small intestine than from the colon ($P < 0.001$).

Concentrations of glutamine and glutamate in tissues

All mucosal tissues of the GI tract contained substantial amounts of both amino acids with concentrations up to fivefold higher than plasma levels (Table 3). Glutamine concentrations were highest in the oesophagus and large intestine but lower in the stomach and small intestine. The glutamine : glutamate ratio varied between tissues, with the oesophagus being the only tissue in which glutamine constituted the major part. In the stomach and large intestine, the ratio was roughly equal, but in the small intestine, glutamate predominated with a value close to 3.

Discussion

This study provides the most complete information available on the distribution of glutaminase and glutamine synthetase throughout the GI tract of the rat. It demonstrates that glutaminase activity is greatest in the mucosa of the small intestine (see also Pinkus & Windmueller, 1977), but is virtually absent from non-mucosal tissues including the mouth and oesophagus. When expressed as total activity, the mucosa of the small intestine, which comprises approximately 50 % of the total weight of the GI tract, contains over 80 % of glutaminase activity. The low level of glutaminase found in the stomach is in keeping with arterio–venous exchange studies. Anderson & Hanson (1983) found that the mean extraction of glutamine by the stomach was only 4·7 % compared with 35 % extraction reported for the small intestine (Windmueller & Spaeth, 1975) even though blood flow through the two tissues is similar. Furthermore, uptake of glutamine by the stomach was much lower than uptake of glucose by this tissue, whereas these two substrates are metabolized at similar rates in the jejunum of post-absorptive rats (Elia, 1996). These data all suggest that the stomach is a far less avid user of glutamine than the small intestine.

The low glutaminase activities observed in the mucosa of mouth and oesophagus may explain the failure of oral glutamine administration to improve mucositis of the upper GI tract. The use of glutamine in this manner was at least partly based on the assumption that these tissues, like the small intestine, possessed the enzymic machinery to utilize glutamine. The current results show that this is clearly not the case. Moreover, the rather low activity of glutaminase in the colonic mucosa may be relevant to the lack of effect of glutamine enemas in experimental colitis in the rat (Neilly *et al.* 1995), although enzyme activities in the diseased colon need to be established.

Glutamine synthetase activity was extremely low in both mucosal and non-mucosal tissue from the small intestine and in the mouth and oesophagus. The colon had slightly higher activity, but only the lower part of the stomach contained significant amounts of glutamine synthetase. The specific activity observed there (about 35 nmol glutamine synthesized /min per mg protein), was considerably higher than is found in muscle (see Table 4) and accounted for more than 90 % of the total synthetase activity in the GI tract. The significance of the high activity of this enzyme in the lower part of the stomach is unknown. Despite the high synthetase activity, intracellular glutamine concentration was low and similar to that seen in the small intestine. This suggests either that the synthesized glutamine is being rapidly utilized, possibly by pathways not involving glutaminase (as glutaminase activity was low in the stomach), or that it is being transported out of the tissue. Glutamine has been reported to be beneficial in healing stomach and duodenal ulcers in man (Shive *et al.* 1957), and preventing aspirin-induced peptic ulceration in rats (Okabe *et al.* 1975); results which clearly suggest that glutamine has an important and as yet unexplained role in this situation.

Table 3. Concentrations of free glutamine and glutamate (mmol/kg wet weight) in mucosal tissues of the gastrointestinal tract and in plasma of rats

(Mean values and standard deviations)

		Glutamine		Glutamate	
Tissue	*n*	Mean	SD	Mean	SD
Oesophagus	6	3·38	0·49	2·19	0·44
Stomach	6	0·89	0·18	1·13	0·27
Small intestine	9	1·04	0·29	2·72	1·28
Large intestine	9	1·92	0·44	1·82	0·41
Blood plasma	6	0·63	0·08	0·12	0·03

Table 4. Total glutaminase and glutamine synthetase activities in various organs of the rat*

		Total activity (μmol/min per whole organ)	
Organ	g tissue/100 g body wt	Glutaminase	Glutamine synthetase
Muscle	40	0·7	15·9
Liver	4·67	38·1	55·0
Kidney	0·88	35·4	3·5
Lung	0·74	4·1	6·9
GI tract	2·44	24·8	2·5

GI, gastrointestinal.

*Organ weights (expressed as g/100 g body weight) were taken from the data of Jennings & Elia (1996). Enzyme specific activities were taken from the data of Lund (1970), King *et al.* (1983), Watford *et al.* (1984), Ardawi (1987*a*,*b*, 1988*a*, 1991), Ardawi & Jamal (1990), Girard & Butterworth (1992). Data from rats weighing between 150 and 300 g were used in the calculations.

The total (mucosal plus non-mucosal) activities of glutamine synthetase and glutaminase in the GI tract relative to those in other tissues are shown in Table 4 which has been constructed using data from the present and other studies. It suggests that the GI tract is one of the major sites of glutamine utilization in the body. In the rat, glutaminase activity in the whole of the GI tract was 24·8 μmol glutamine hydrolysed/min, compared with activities of 38·1 and 35·4 μmol/min in the whole liver and kidneys respectively. These latter two tissues are known to utilize glutamine in, for example, urea detoxification and maintenance of acid–base homeostasis, but much of the glutamine used is synthesized within the tissue. On the other hand, overall glutamine synthetase in the gut is insignificant compared with other organs of the body (Table 4). Although the specific activity of glutamine synthetase in the stomach is some 10–15 % higher than in muscle, total activity in the GI tract is only 2·5 μmol glutamine synthesized/min, considerably less than 55·0 μmol/min produced by the liver and 15·9 μmol/min synthesized in the musculature. These data highlight the fact that the GI tract as a whole is heavily dependent on an external source of glutamine and has only a very limited ability to synthesize this amino acid.

Using the methods described, the total activity of glutaminase in the GI tract of the rat is approximately 24 μmol glutamine hydrolysed/min, i.e. some 30–40-fold greater than the net uptake of glutamine (600–700 nmol/min) measured by arterio–venous techniques (Windmueller & Spaeth, 1974). The discrepancy between the *in vivo* rate of uptake and *in vitro* glutaminase activity can in part be attributed to the difference between *in vivo* glutamine concentrations and the concentration of glutamine used in the *in vitro* assay. The observed K_m of the enzyme from the small intestine in this study was 2·67 mM, a value similar to that quoted by other groups (Pinkus & Windmueller, 1977; Hortelano *et al.* 1991*a*,*b*; Salloum *et al.* 1991). This value indicates that the glutamine concentration used in the enzyme assay (4 mM) is approximately 25 % below the concentration required for maximum enzyme activity in this tissue. On the other hand, 4 mM would allow maximum activity in the colon, where a lower K_m value of 1·69 mM was found. Glutamine concentrations *in vivo* however, are generally well below these values. The plasma concentration of glutamine is about 0·5 mM and in man, lumenal concentrations are reported to reach 1·2 mM following a protein-rich meal. Clearly such concentrations are below those needed for maximal enzyme activity. It is also likely that glutaminase activity will be influenced by local factors such as pH, and the presence of enzyme activators, such as phosphate, and inhibitors, such as glutamate.

Concentrations of glutamine and glutamate and their relative proportions varied in different parts of the GI tract. The small intestine had the greatest glutamate : glutamine ratio, in keeping with the high glutaminase activity in this tissue. The roughly equal glutamate : glutamine ratio in the stomach and large intestine match the lower glutaminase activity in these tissues, and the very high concentrations of both glutamine and glutamate in the oesophagus are also consistent with the very low activities of both enzymes in this tissue.

In summary, this study provides the first systematic examination of the distribution of glutamine synthetase and glutaminase in mucosal and non-mucosal tissues in different parts of the GI tract of the rat. Three major conclusions have emerged. First, the results confirm that the small intestine, and particularly the mucosal layer, has by far the greatest potential for glutamine utilization throughout the GI tract. Second, it is clear that the stratified squamous epithelium of the mouth and oesophagus has very little potential to either synthesize or utilize glutamine. Finally, with the exception of the lower stomach, tissues in the GI tract of the rat have little capacity for synthesizing glutamine and consequently glutamine requirements of the tissues must be met either from the diet or via endogenous production in other parts of the body.

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