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Is there a correlation between taurine levels and xenobiotic-induced perturbations in protein synthesis?: A study with tetracycline in rats

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Summary. Changes in urinary levels of taurine have been reported in rats following treatment with various xenobiotics including those which alter protein synthesis and/or are hepatotoxic. This paper reports on the time course of the urinary elevation of taurine following treatment of rats with tetracycline (50, 150 and 200 mg.kg^{-1}). Maximum taurine excretion occurred 8–12 h following dosing. Serum albumin and total protein were significantly lower after 24 h (200 mg.kg^{-1}). The increase in urinary taurine was dose-related and reflected in the raised serum levels of taurine 24 h after dosing. Serum and urinary protein and [^{3}H]-leucine incorporation into acid precipitable protein in liver and muscle were reduced by tetracycline (100, 150 and 200 mg.kg^{-1}) 10 h after dosing. The reduction in protein synthesis was correlated with increased urinary and serum levels of taurine at 10 h. The use of taurine as a non-invasive marker of protein synthesis is discussed.

Keywords: Amino acids – Taurine – Protein synthesis – Urinary marker – Tetracycline – Glutathione

Introduction

We have previously shown that many hepatotoxic compounds such as those which cause necrosis (eg. carbon tetrachloride, thioacetamide and galactosamine) and those which cause fatty liver (steatosis) (eg. ethionine and hydrazine) result in elevated levels of urinary taurine (Waterfield et al., 1993a). All of these compounds inhibit protein synthesis; a feature of hepatotoxicity. Subsequently, we have shown that after dosing with the β-agonists salbutamol (Carvalho et al., 1995) and clenbuterol (Waterfield et al., 1995) (which increase protein synthesis), or cycloheximide (Waterfield et al., 1996) (which reduces protein synthesis) levels of urinary taurine were significantly decreased or increased respectively. Inhibition of protein synthesis will

result in an accumulation of amino acids including cysteine, the precursor of taurine, both from dietary sources and those resulting from protein degradation. There were significant correlations in these studies between protein synthesis measured as the incorporation of [^{3}H]-leucine into acid precipitable proteins and taurine levels in serum and urine following both clenbuterol and cycloheximide treatment of rats.

In order to monitor the rate of protein synthesis using radiolabelled amino acids, it must be decided either to administer a pulse dose given 10 min before necropsy or to use continuous infusion (Garlick et al., 1980; Preedy et al., 1990). The choice of amino acid, the time at which to measure the incorporation of radiolabelled amino acid into protein, the size of the endogenous unlabelled precursor pool and the rate of protein degradation all lead to difficulties in assessing any effects a compound may have on protein synthesis (Rannels et al., 1982; Garlick et al., 1994). All of the *in vivo* methods used are invasive techniques often requiring the sacrifice of animals. For pulse labelling, the time course for the inhibition of protein synthesis also needs to be determined in advance before measuring the reduction in tracer incorporation into proteins. We have suggested that measuring urinary taurine levels could be a useful non-invasive method for monitoring changes in protein synthesis brought about by a variety of different mechanisms (Timbrell et al., 1995).

The tetracyclines are broad spectrum antibiotics used to treat a number of infections such as those of the respiratory and urinary tracts. Their selective microbial action is based on their uptake by bacterial cells which is much greater than by human cells. Tetracycline binds to the 30s ribosomal subparticle resulting in the inhibition of translocation of phenylalanyl-tRNA from donor to receptor site (Igarashi and Kaji, 1970; Last, 1969). Thus, the mechanism of protein synthesis inhibition is different from the other compounds we have investigated with respect to changes in taurine levels. Tetracyclines also cause a dose-dependent accumulation of triglycerides (microvesicular steatosis) in animal studies (Estler and Böcker, 1980). This results from an inhibition of triglyceride secretion which takes place in the absence of any effect on triglyceride synthesis (Breen et al., 1972; 1975; Deboyser et al., 1989).

The aim of the current studies was to follow the urinary excretion of taurine after the administration of different doses of tetracycline to rats and correlate this with any change in the incorporation of [^{3}H]-leucine into acid precipitable proteins.

Materials and methods

Chemicals

The following compounds were supplied by the Sigma Chemical Company (Poole, Dorset, U.K.): tetracycline hydrochloride, o-phthalaldehyde (OPA; HPLC grade), taurine (cell culture tested), Dowex resins, 5,5′-dithiobis-2-nitrobenzoic acid (DTMB) for measurement of total non-protein sulphydryls (TNPSH), glutathione, L-leucine and bovine serum albumin. Mercaptoethanol, sodium hydroxide (Aristar), sulphosalicylic acid,

boric acid and Folin's reagent were obtained from Merck Ltd. (Lutterworth, Leicestershire, U.K.); methanol (HPLC grade) from Rathburn (Wakeburn, Scotland, U.K.). Coomassie Plus Protein Assay Reagent, for measurement of urinary protein, was purchased from Pierce and Warriner, Chester, U.K. Water was of ultra high quality (UHQ), prepared using an Elgastat water purifier. Other chemicals were Eco-lite from ICN Biochemicals Ltd. (Thame, Oxfordshire, UK) and L-[4,5-^{3}H]-leucine (52 Ci/mmol) from NEN Research products, Dupont (UK) Ltd., Stevenage, Herts, UK.

Animals and husbandry

Studies used male rats (Han-Wistar stock GlaxoWellcome Research and Development, Ware), weighing 217–262 g (study 1) and 209–224 g (study 2). They were acclimatised for eight days in communal cages after delivery then housed in individual metabolism cages during the studies (Waterfield et al., 1995). The rats were allocated to treatment groups (4 in each group), with the same mean body weights. Powdered diet 41B (Special Diet Services, Witham, Essex, UK) and drinking water were allowed *ad libitum*. Lighting was controlled to give a regular 12 h light-dark cycle (8 am on–8 pm off) and room temperature was maintained at 21 ± 1°C. Animals were allowed to acclimatise to the metabolism cages for 3 days during which time food and water intake were monitored and animals weighed.

Three (study 1) or two (study 2) predose urine collections (24 h) were made over ice, and diluted to 25 ml with UHQ water and stored in 5 ml aliquots at −80°C for later analysis.

As previous studies have shown a correlation between alterations in protein synthesis and changes in urinary taurine levels the first study (study 1) was carried out to establish the time of maximum elevation in urinary taurine levels following tetracycline administration in order to target the best time for radio-labelling proteins.

Study 1

At 10 am, animals were dosed with 0, 50, 150 or 200 mg.kg^{-1} tetracycline (free base) in phosphate buffered saline (8 ml.kg^{-1} ip, pH adjusted to 6.0 with HCl) (Michael et al., 1961; Breen et al., 1975). Urine collections were made 0–4, 4–8, 8–12 and 12–24 h after dosing. After 24 h animals were anaesthetised, exanguinated from the abdominal aorta and tissues taken as described below.

Study 2

After analysis of the data from study 1, a second study was carried out. Four groups of rats (4/group) were housed in individual metabolism cages and 24 h pre-dose urine collections were made as before. Results from study 1 indicated that there was a rise in urinary taurine between 4 and 8 h after dosing with tetracycline (Fig. 1) which may have been maximal between 8 and 12 h. Animals were therefore dosed at 7 minute intervals with tetracycline (0, 100, 150 or 200 mg.kg^{-1} free base, as before). The lowest dose of tetracycline was raised in the second study as 50 mg.kg^{-1} failed to show any effect in the first study. Food was withdrawn from animals as data from study 1 indicated that 150 and 200 mg.kg^{-1} tetracycline reduced the intake of food in these two groups (Fig. 2B). Eight hours later and 2 h before post mortem, a single dose of [^{3}H]-leucine given to each animal (400 μCi, 200 μmol.kg^{-1}, in 4 ml, ip).

Two urine collections were made; 0–5 h and 5–10 h after dosing with tetracycline.

Blood and tissue sampling

At the end of both studies, animals were anaesthetised (Hypnorm:Hypnoval:water; 1:1:2, 3.33 ml.kg^{-1} ip) and exsanguinated from the abdominal aorta. Blood was collected

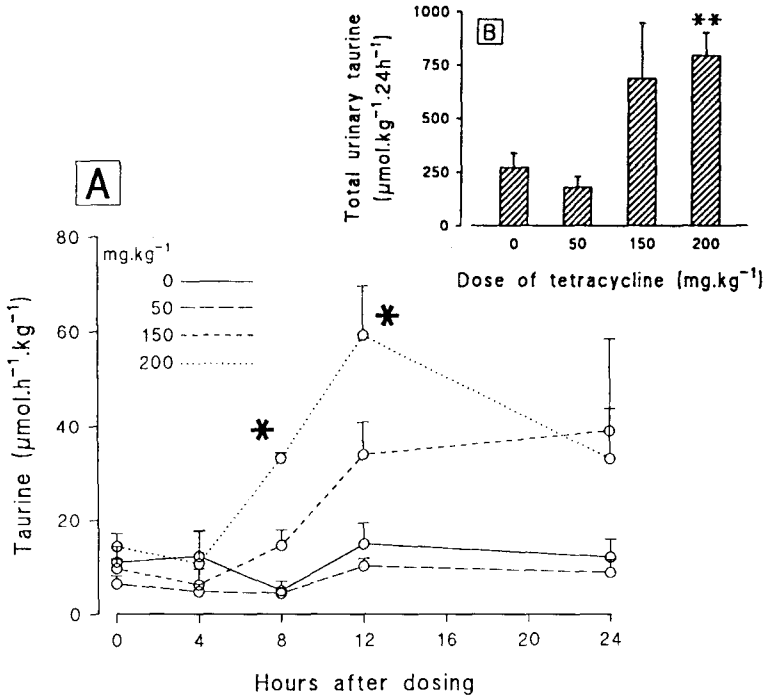

Fig. 1. **A** Taurine excretion in urine collections made over 24h following treatment of rats with tetracycline. Values are means ± sem for each point; N = 4; *p < 0.05 value compared with pre-dose urinary excretion of taurine using paired "t" test. **B** Total urinary excretion of taurine 24h after dosing; N = 4; **p < 0.01, Dunnett's test

into Microtainer serum separators (Beckton Dickinson and Co., Rutherford, NJ, USA) and centrifuged (13,000g, 1min) to separate the serum which was frozen until analysed (−80°C). The gastrocnemius muscle and liver were removed, weighed and the right liver lobe and muscle were frozen in liquid nitrogen for subsequent analysis of taurine, total non-protein sulphydryl groups (TNPSH), protein and incorporation of [^{3}H]-leucine into acid precipitable protein. Tissues were stored at −80°C until analysed. A section of liver and the kidneys were taken into 10.5% phosphate buffered formaldehyde and prepared for histology as previously described (Waterfield et al., 1991).

Serum chemistry

Any tissue damage resulting from the treatment was assessed by measuring serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) lactate dehydrogenase (LDH), alkaline phosphatase (ALP), glutamate dehydrogenase (GLDH) (study 2 only), albumin, total protein, glucose, total bilirubin, cholesterol, bile acids, urea, triglycerides and creatinine and other parameters at 37°C, using the appropriate kits (Boehringer Mannheim GmbH Diagnostica) with a centrifugal analyzer (IL Monarch 2000, Instrumentation Laboratory, UK. Ltd).

Taurine and total non-protein sulphydryls (TNPSH)

Taurine was extracted from diluted urine (25 μl) using Dowex resins similar to the method previously described (Waterfield, 1994) modified from Larsen et al. (1980) using homoserine as internal standard. Taurine and TNPSH were measured in the supernatants

from liver and skeletal muscle homogenates (300mg in sulphosalicylic acid 0.2M, 4ml, 4°C) (Waterfield, 1994; Ellman, 1959). As reduced glutathione (GSH) constitutes >95% of liver and muscle TNPSH, this was used as a measure of GSH (DeMaster and Redfern, 1987; Potter and Tran, 1993). Serum taurine was measured in acid extracts after deproteinating serum samples (200μl) with sulphosalicylic acid (200μl, 0.4M, 11,000g, 4°C). Taurine was measured using fluorimetric detection in the eluates from the ion exchange columns using HPLC after derivatisation with OPA and mercaptoethanol.

[^{3}H]L-leucine incorporation into protein

[^{3}H]L-leucine incorporation into acid precipitable proteins from liver, skeletal muscle and serum was measured in the sulphosalicylic acid precipitated protein pellets prepared when making acid extracts for taurine and TNPSH measurements as previously described (Waterfield et al., 1996).

Urinary protein

Urinary protein was measured in diluted urine (1 + 99) and assayed for protein using Coomassie Brilliant Blue G-250 (Pierce Protein Assay Reagent) and a microassay procedure. The absorbency was determined at 595nm and compared to bovine serum albumin standards (0–25μg.ml^{-1}).

Statistical analysis

Urinary levels of taurine in samples taken from the same animal on different days were compared with pre-dose values for each animal using a paired Students "t" test. For all other data, Dunnett's test for multiple comparisons with a single control was used to determine significance between treatment groups and the control group.

Results

Body weights, food and water intake

Study 1

Animals treated with both 150 and 200mg.kg^{-1} tetracycline ate significantly less food than the other two groups (Fig. 2B). Body weight and water intake were similar in all groups although animals treated with 150 and 200mg.kg^{-1} tetracycline did show a slight, but not significant, weight loss (Figs. 2A and 2C).

Study 2

There was no significant effect on body weight or water intake 10h after dosing in any of the treatment groups (data not shown). Food was withdrawn after dosing.

Organ weights

Liver weights were lower in animals 24h after dosing with 200mg.kg^{-1} of tetracycline (absolute and expressed % bodyweight, Fig. 3A) but not signifi-

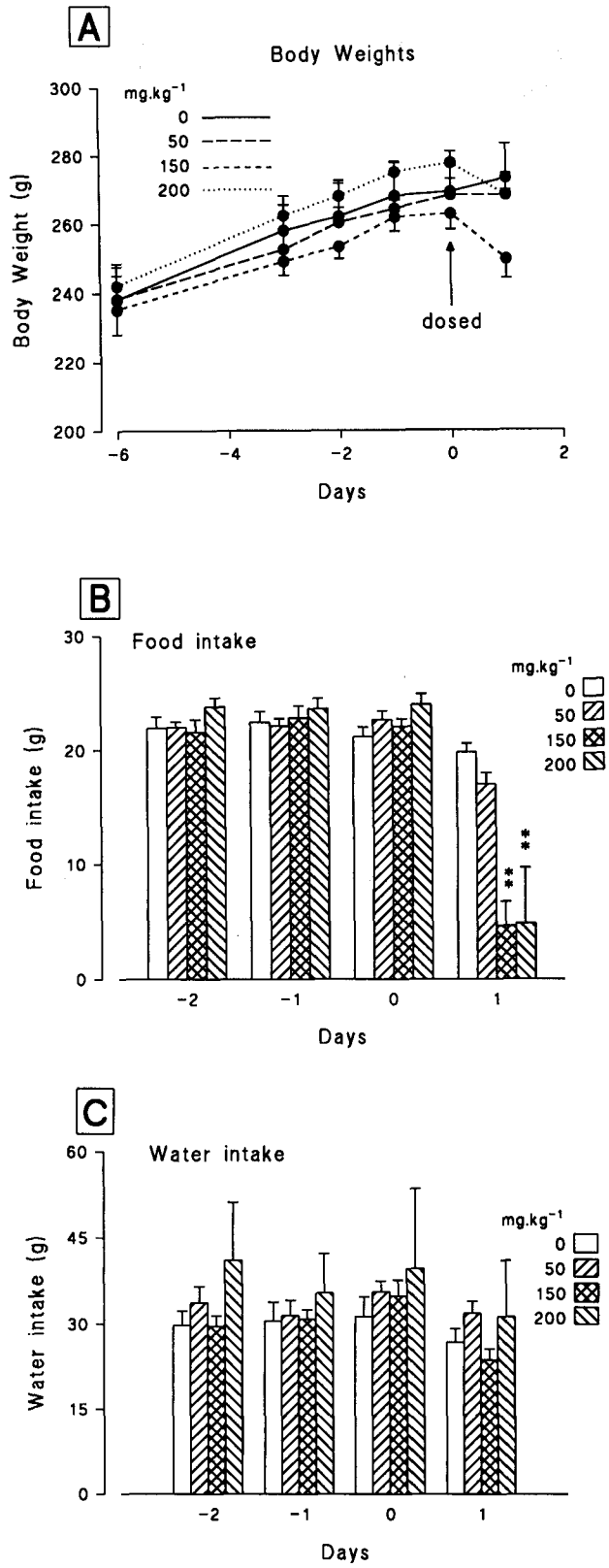

Fig. 2. Study 1. **A** Body weights, **B** food, and **C** water intake in animals before and 24 h following dosing with tetracycline. Values are means ± sem; N = 4; **p < 0.001, Dunnett's test

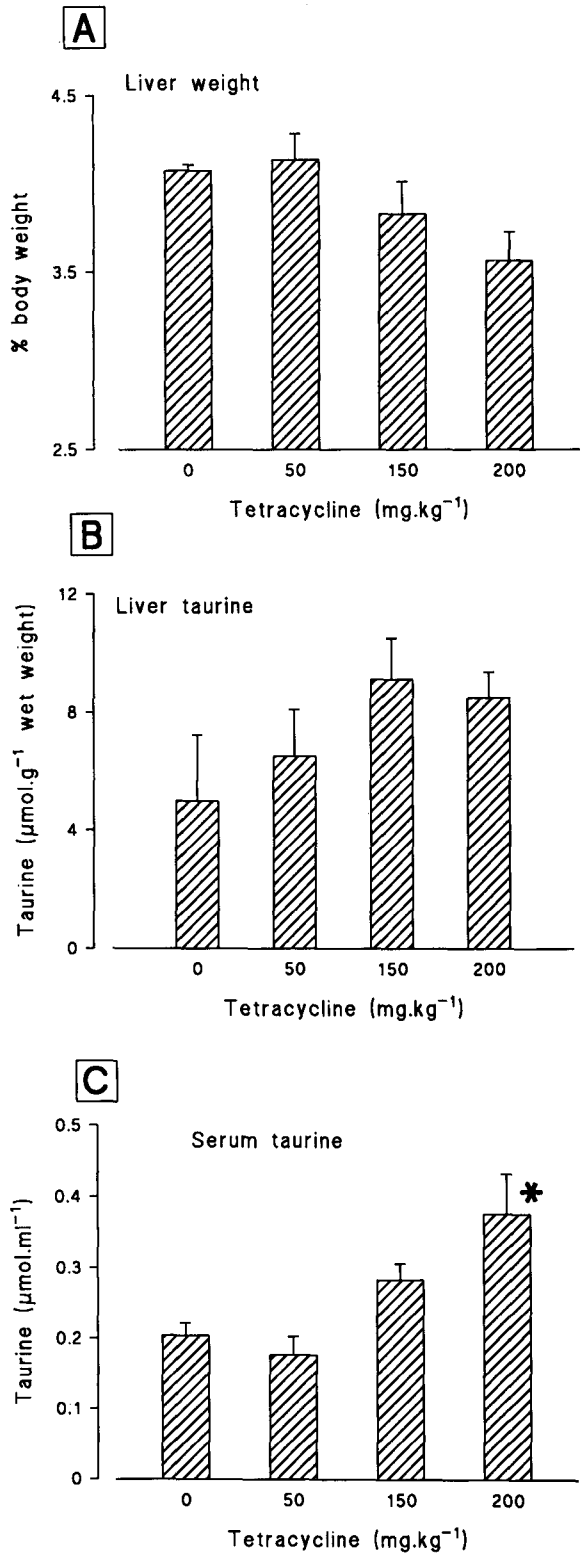

Fig. 3. Study 1. **A** Liver weights (% body weight), **B** concentration of taurine in the liver (μmol.g^{-1} wet weight of tissue), **C** serum taurine concentration (μmol.ml^{-1}) measured in rats 24 h after treatment with tetracycline. Values are means ± sem; *$p < 0.05$ using Dunnett's test

cantly (study 1). There was no difference in liver weights in study 2, 10 h after dosing. Kidney weights were the same in all groups, in both studies (data not shown).

Serum chemistry

Study 1

Total serum proteins and serum albumin were both significantly reduced by the highest dose of tetracycline and AST levels were raised after 150 and 200 mg.kg^{-1} tetracycline as was creatinine after 150 mg.kg^{-1}. There was also a very significant reduction in serum triglyceride levels and a reduction in serum cholesterol (Table 1A). Other serum parameters were unchanged by the treatment (data not shown).

Study 2

None of the serum parameters measured 10 h after dosing were significantly different from control values although serum protein, AST and triglycerides did show a similar trend to the results in study 1 (Table 1B). Serum urea nitrogen and glutamate dehydrogenase (GLDH) also showed a dose-dependent increase, but again the levels were not significantly different from control values.

Taurine levels

Urinary taurine

Study 1. Urinary taurine was raised above control levels by 150 and 200 mg.kg^{-1} tetracycline 4–8 h and 8–12 h after dosing, but only significantly after the highest dose (Fig. 1A). Levels were still raised in the 12–24 h collection but not significantly different from control or starting values. Total urinary excretion of taurine 24 h after treatment is also shown (Fig. 1B).

Study 2. Urinary taurine was raised 5–10 h after all three doses of tetracycline although there was considerable variation in the results (Fig. 4A) and there was a significant correlation between serum taurine and the urinary taurine excreted 5–10 h after dosing the animals with tetracycline as would be expected (Fig. 4B).

Hepatic, skeletal muscle and serum taurine

Liver taurine concentrations were raised but not significantly different from the control group of animals 24 h after dosing animals with all doses of tetracycline (Fig. 3B) and serum taurine concentrations were significantly raised by 200 mg.kg^{-1} tetracycline (study 1, Fig. 3C). Taurine was not

Table 1A. Serum clinical chemistry 24 h after dosing rats with tetracycline

Tetracycline ($mg.kg^{-1}$)	AST (iu/L)	Albumin ($g.L^{-1}$)	Total protein ($g.L^{-1}$)	Creatinine ($\mu mol.L^{-1}$)	Triglycerides ($mmol.L^{-1}$)	Cholesterol ($mmol.L^{-1}$)
0	73 ± 5	35 ± 0.7	53.4 ± 1.2	60.0 ± 1.1	0.82 ± 0.09	1.45 ± 0.10
50	75 ± 9	35.6 ± 0.4	55.0 ± 0.4	62.3 ± 0.8	0.64 ± 0.03	1.36 ± 0.02
150	258 ± 53*	32.5 ± 0.7	48.7 ± 1.3	71.0 ± 4.0*	0.22 ± 0.03***	0.85 ± 0.17
200	281 ± 102*	30.1 ± 2.3*	43.8 ± 4.2*	67.3 ± 3.7	0.25 ± 0.03***	0.66 ± 0.28*

Table 1B. Serum clinical chemistry 10 h after dosing rats with tetracycline

Tetracycline ($mg.kg^{-1}$)	AST (iu/L)	Albumin ($g.L^{-1}$)	Total protein ($g.L^{-1}$)	Creatinine ($\mu mol.L^{-1}$)	Triglycerides ($mmol.L^{-1}$)	Cholesterol ($mmol.L^{-1}$)	Serum urea ($mmol.L^{-1}$)	GLDH ($iu.L^{-1}$)
0	58 ± 6	29.2 ± 1.0	51.0 ± 1.0	39.3 ± 1.8	0.32 ± 0.04	1.11 ± 0.11	3.2 ± 0.1	5.0 ± 0.6
100	162 ± 71	26.7 ± 0.9	46.0 ± 3.0	39.2 ± 3.1	0.27 ± 0.02	0.99 ± 0.11	6.0 ± 1.9	18.5 ± 10.1
150	236 ± 87	26.6 ± 2.0	44.0 ± 4.0	42.3 ± 3.5	0.32 ± 0.38	0.82 ± 0.24	8.2 ± 2.8	22.5 ± 6.4
200	310 ± 136	25.3 ± 1.0	42.0 ± 2.0	61.8 ± 23.1	0.23 ± 0.04	0.67 ± 0.20	12.8 ± 6.3	24.3 ± 9.8

Values are means ± s.e.m. *$p < 0.05$ and ***$p < 0.001$ Dunnett's test for multiple comparisons with a single control. *AST* aspartate amino transferase; *GLDH* glutamate dehydrogenase.

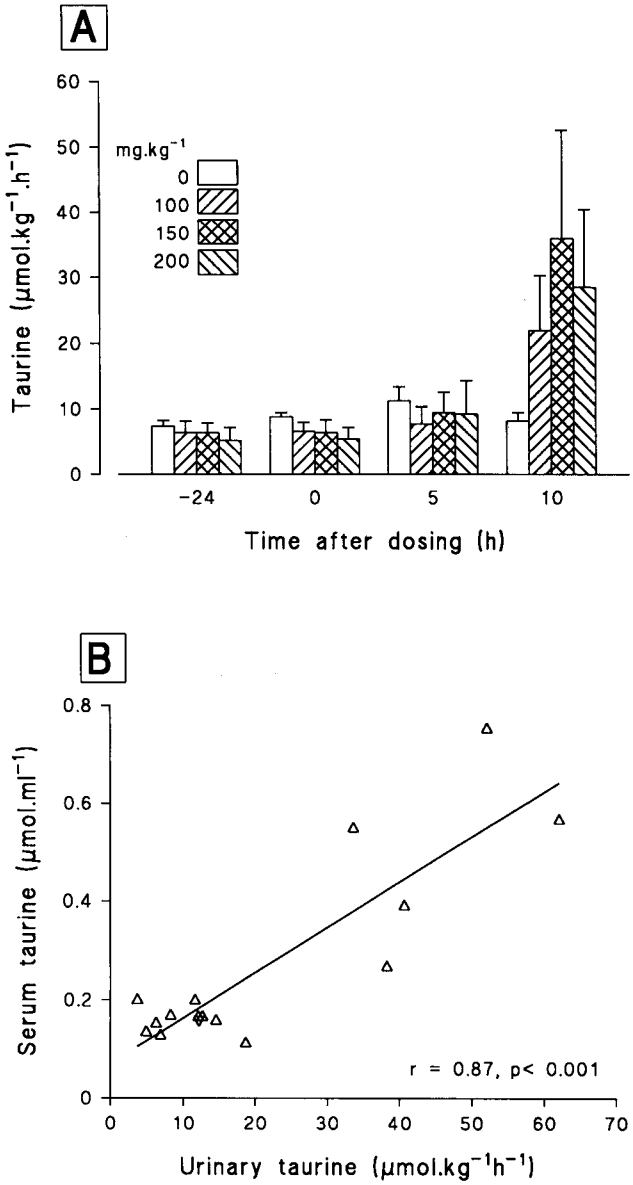

Fig. 4. Study 2. **A** Urinary excretion of taurine following dosing with tetracycline; values are means ± sem; N = 4. **B** Correlation between individual serum taurine levels and urinary taurine excreted 5–10 h following dosing. Each point represents data from an individual animal; N = 16

measured in skeletal muscle 24 h after dosing. However, the concentrations of taurine in the liver, muscle and serum taken 10 h after dosing were not significantly different from control values although serum taurine concentrations did appear to be raised in some animals (study 2, Table 2).

Table 2. Taurine levels and [^{3}H]-leucine incorporation into acid precipitable proteins from tissues taken 10h after dosing with tetracycline (study 2)

Tetracycline ($mg.kg^{-1}$)	Liver taurine ($\mu mol.g^{-1}$)	Muscle taurine ($\mu mol.g^{-1}$)	Serum taurine ($\mu mol.ml^{-1}$)	[^{3}H]-leucine incorporation into protein ($dpm.mg^{-1}$)		
				Liver	Muscle	Serum
0	10.63 ± 1.97	15.55 ± 0.38	0.16 ± 0.02	51798 ± 2954	3095 ± 148	157 ± 11
100	7.66 ± 1.02	12.60 ± 0.74	0.29 ± 0.09	45571 ± 6486#	2726 ± 105#	160 ± 13#
150	7.76 ± 1.41	15.10 ± 0.85	0.31 ± 0.10	42216 ± 5138	2037 ± 352*	180 ± 23
200	8.55 ± 2.77	14.97 ± 0.81	0.63 ± 0.35	38322 ± 4150*	1920 ± 456*	180 ± 9

Values are means ± sem; N = 4, except # where N = 3; *$p < 0.05$, (Dunnett's test).

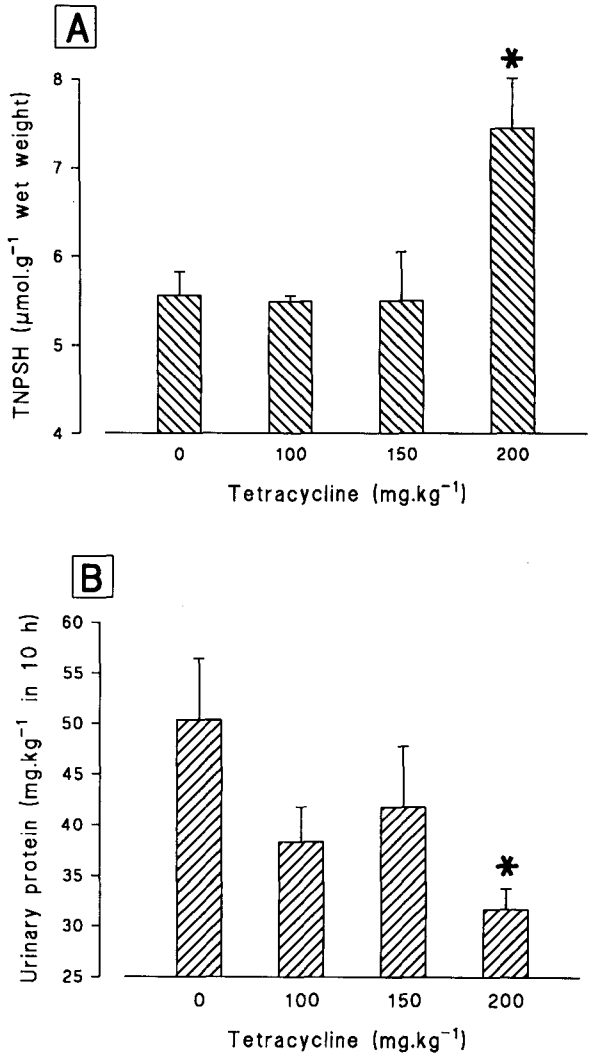

Fig. 5. Study 2. **A** Liver total non-protein sulphydryls (TNPSH) measured in liver 10 h after dosing animals with tetracycline. Values are means ± sem; *$p < 0.05$, Dunnett's test. **B** Total urinary protein excreted for 10 h following dosing with tetracycline ($mg.kg^{-1}$). Values are means ± sem; *$p < 0.05$

Hepatic total non-protein sulphydryls (TNPSH)

Total non-protein sulphydryl levels were unchanged in liver tissue taken 24 h after dosing. There was, however, a significant increase 10 h after treatment with 200 $mg.kg^{-1}$ tetracycline (Fig. 5A).

Urinary protein

Total urinary protein (0–10 h post-dose) was reduced in all animals treated with tetracycline in study 2. The results were significantly different from control urines after 200 $mg.kg^{-1}$ tetracycline (Fig. 5B).

[^{3}H]-Leucine incorporation into protein

Study 2. There was a significant dose-dependent reduction in the amount of [^{3}H]-leucine incorporated into acid precipitable protein in both the liver and muscle tissue 10h after dosing animals with tetracycline but no difference was seen in serum proteins (Table 2). Figures 6A–6D show that there was a correlation between the reduction of [^{3}H]-leucine incorporation into liver and muscle proteins and increased levels of both serum taurine and total urinary taurine excretion following dosing.

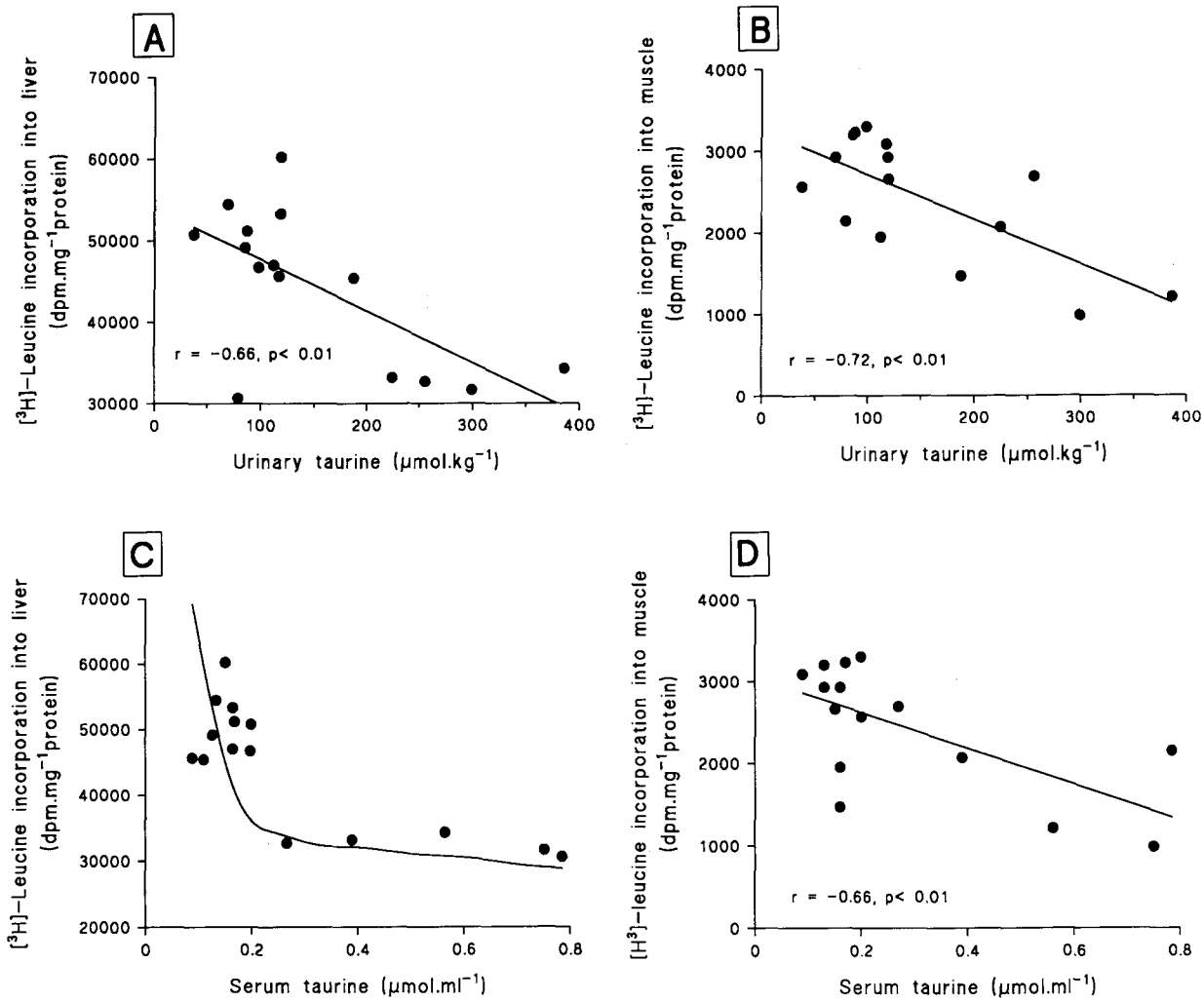

Fig. 6. Study 2. Correlation between total urinary excretion of taurine following dosing (0–10h) and [^{3}H]-leucine incorporation into acid precipitable protein; **A** liver, **B** muscle. Correlation between serum taurine concentrations 10h after dosing and [^{3}H]-leucine incorporation into acid precipitable protein; **C** liver, **D** muscle. Each point represents data from a single animal; N = 15. (One animal was miss-dosed with [^{3}H]-leucine in 100mg.kg^{-1} group)

Discussion

The aim of these investigations was to assess how accurately tissue and urinary levels of taurine would reflect and/or correlate with the incorporation of [^{3}H]-leucine into acid precipitable proteins, as a measure of protein synthesis. The inhibition of protein synthesis and subsequent increase in amino acid levels are a feature of hepatotoxicity which can occur in the absence of overt cellular damage. This inhibition may underlie triglyceride accumulation in the liver (Dianzani, 1991). Raised levels of serum AST 24 h post-dosing with 150 and 200 mg.kg^{-1} tetracycline indicated that there may have been tissue damage although the lack of elevation of ALT and the slight (but not significant) rise in GLDH (study 2) suggested that liver injury was minimal. Histopathological changes in the liver were not evident by light microscopy.

As urinary taurine was being investigated as a potential marker of changes in protein synthesis, it was important to establish whether tetracycline (a) caused kidney injury and (b) inhibited protein synthesis. There was a slight, but not significant rise in both serum creatinine (10 and 24 h post-dose) and urea (10 h post-dose) which may have reflected impaired kidney function. However, the significant reduction in urinary protein 10 h following dosing rats (which normally excrete high levels of urinary protein) suggested that this was not the case. The rise in serum urea is also consistent with a change in protein status resulting in the deamination of excess amino acids as a result of changes in amino acid utilisation in protein synthesis. These changes are therefore consistent with an inhibition of protein synthesis being brought about by tetracycline. Absolute protein values were measured in serum and urine. Both albumin and total serum protein were significantly reduced, 24 h after treatment with 200 mg.kg^{-1} tetracycline. There was a dose-dependent reduction in [^{3}H]-leucine incorporation into acid precipitable protein in liver and muscle 10 h after dosing. There was however, no difference in the incorporation of [^{3}H]-leucine into serum acid precipitable proteins. Serum albumin and total protein were reduced, 10 h after treatment and by 24 h these decreases were significant. Measurement of [^{3}H]-leucine incorporation into serum proteins, may have been carried out too early to show a change in incorporation.

Urinary taurine was significantly elevated 4–12 h after dosing with tetracycline (study 1) and was elevated 5–10 h after dosing in study 2. This was despite the fact that the treated animals had a significant reduction in their food intake at the highest doses (study 1). Reduced food intake would normally reduce urinary output of taurine (Waterfield et al., 1993b). The removal of food in study 2 did not prevent the rise in urinary taurine which was seen between 5 and 10 h following dosing, although there was considerable variation in the results.

The significantly reduced levels of serum triglycerides found 24 h after dosing rats with 150 and 200 mg.kg^{-1} tetracycline suggests that transport of triglycerides out of the liver had been inhibited by the treatment (Breen et al., 1975; Deboyser et al., 1989). However, the reduced intake of food in these two

groups of animals compared to the control group may also have contributed to the reduction as fasted levels (study 2) were similar to the treated levels from study 1 (Tables 1A and 1B) (Robinson and Evans, 1996). Fasted levels (study 2) of serum cholesterol were also similar to the values obtained from the treated groups (study 1) which may therefore reflect nutritional status rather than an effect of tetracycline.

The data presented here for hepatic TNPSH (which includes GSH) showed that there was an increase 10 h after dosing with tetracycline (study 2) despite the fact that the animals had been starved for 10 h. The liver TNPSH concentration in the animals given 200 mg.kg^{-1} was as high as those found in replete animals. TNPSH levels measured in animals 24 h after treatment were all similar to control levels. This level may have been higher in animals treated with both 150 and 200 mg.kg^{-1} tetracycline than expected as they had a reduced food intake. The results could therefore, reflect an actual increase in GSH synthesis due to raised cysteine levels following the inhibition of protein synthesis.

The levels of liver taurine 10 h after dosing were similar to control levels and were slightly, but not significantly elevated. Liver levels of taurine do vary more than those in any other tissue (Hirai et al., 1987) probably due to the effects of bile acid conjugation and biliary excretion as well as the rate of transportation into the blood stream to other tissues. The variation in serum taurine levels following tetracycline treatment suggested that there had been an effect of the compound on the levels but the effect was not consistent. Liver taurine has a short half life and excess serum taurine is rapidly excreted in the urine. Thus, urinary taurine may better reflect an increase in the body pool of taurine.

These data reinforce the hypothesis, made in previous studies, that the hypertaurinuria which develops in rats treated with some hepatotoxic compounds is either increased by the inhibition of protein synthesis (eg. CCl_4 and galactosamine) or is a direct result of the inhibition (eg. hydrazine and ethionine) (Waterfield et al., 1993a). As there appears to be a good correlation between the incorporation of leucine into protein and the urinary excretion of taurine, the measurement of urinary taurine may provide a useful non-invasive method for monitoring the effects of xenobiotics or other stress induced alterations in protein synthesis such as surgical trauma.

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