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ACUTE HEPATIC EFFECTS OF LOW-DOSE FUMONISIN B_1 IN RATS

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Adult male Wistar rats were enrolled in a study to test the acute hepatic effects of 50 mg/kg fumonisin B_1 in feed for 5 days. Fumonisin B_1 depressed growth and feed intake, and absolute and relative liver weight showed a significant increase. The proportions of C17:0, C18:3 n3, C22:5 n3 and C22:6 n3 fatty acids decreased in the hepatic phospholipid fraction. All proportional decreases modified the hepatocellular membrane lipids into a more rigid state. The fatty acid profile modifications were partly compensated for by endogenous glutathione (preventing the formation of conjugated dienes and trienes as initial phase lipid peroxidation indicators), while the enzymatic antioxidant defence system (glutathione peroxidase) was unaltered. In contrast, hepatic malondialdehyde, the cytotoxic product of end-phase lipid peroxidation showed a concentration increase even after 5 days of feeding. The results indicate a rather strong and rapid hepatic effect of FB_1, immediately impairing membrane phospholipids, even before the enzymatic antioxidant defence is activated.

Key words: Fumonisin B_1, rat, hepatocellular membrane, fatty acids, oxidative stress, antioxidants

Fumonisins are cancer-inducing metabolites of *Fusarium proliferatum* and *Fusarium verticillioides*. They have a long-chain hydrocarbon unit (mimicking to a certain extent cellular sphingosine and sphinganine), which plays a determinant role in their cell-membrane-associated toxicity. From the fumonisin group, fumonisin B_1 (FB_1) shows strong toxic effects and has been reported to promote hepatic tumour in rats. Fumonisin B_1, the most abundant of the numerous fumonisin analogues, was classified by the IARC as a Group 2B carcinogen (possibly carcinogenic in humans; IARC, 2002).

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Focusing merely on the hepatic effects of FB_1, Gelderblom et al. (2001) reported that in rat liver FB_1 initiates cancer primarily by exerting hepatotoxic effects and through augmented lipid peroxidation. In an earlier study Abel and Gelderblom (1998) reported significantly increased thiobarbituric acid reactive substance (TBARS) level as a result of 250 and 500 mg/kg FB_1 exposure in the feed for 21 days, causing damage to cellular and microsomal membranes as well. Perhaps this was the first hint that FB_1 sensitises hepatocytes toward oxidative stress. As a consequence, emerging free radicals induce hepatocellular damage and metabolic abnormalities. Based on the above information, Abel and Gelderblom (1998) classified FB_1 as a hepatotoxic but non-genotoxic compound in rats. Sahu et al. (1998) studied whether FB_1 affects nuclear membranes and DNA in the rat liver, and confirmed the induction of nucleolemmal lipid peroxidation as well as DNA strand breaks. Interestingly, for the compensation of lipid peroxidation only catalase was found to provide an antioxidant activity increase. Sahu et al. (1998) hypothesised that peroxyl radicals and hydroxyl radicals are responsible for the DNA damage.

Lipid-compositional changes underlying microscopic alterations caused by FB_1 were partly elucidated by Gelderblom et al. (1997) by feeding rats a drastically toxic, cancer-promoting level (250 mg/kg feed) of this toxin. They found altered lipid constituent proportions; in particular phosphatidylethanolamines (PE) were significantly increased in the mitochondrial and even in the plasma membrane fractions. In a recent study on the effects of a 10 mg/kg FB_1 supplementation in the feed of rats for 28 days we confirmed these changes in the fatty acid (FA) composition of the hepatic mitochondrial phospholipids (PL) (Szabó et al., 2016). In the FA profile of the main polar lipid fractions, i.e. phosphatidylcholine (PC) and PE, a decreased arachidonic acid (C20:4 n6) and polyunsaturated/saturated FA ratio was demonstrated, suggesting a less fluid membrane structure. The decreased levels of polyunsaturated fatty acids (PUFA) in PC along with a marked elevation of oleic (C18:1 n9) and linoleic (C18:2 n6) acids were indicative of an impaired $\Delta 6$ desaturase activity. The authors concluded that FB_1 disrupts sphingolipid, phospholipid (the effect of a polar toxin molecule on the cellular polar lipid fractions), cholesterol and FA metabolism in the liver, in a manner decreasing membrane fluidity and ultimately leading to apoptosis. It has to be added that all the above-listed cellular-level reactions were attained with the lowest FB_1 dose of 10 and 50 mg/kg fed for a minimum period of 21 days.

As far as the authors are aware, the acute effects of FB_1 have only been tested *in vitro* (24–48 h; Abel and Gelderblom, 1998). Since those settings are hardly comparable with an *in vivo* trial, we aimed to test the acute effects of a relatively low but realistic dose of FB_1 (50 mg/kg feed) using an exposure that lasted for only 5 days. The study included the partial analysis of the initial, propagation and end-phases of lipid peroxidation and the determination of some endogenous antioxidants in rats.

Materials and methods

Animals and feeding

Adult, male Wistar Crl:WI BR rats (8 weeks of age) were enrolled in the study and were kept in metabolic cages (Tecniplast, Castronno, Italy) individually. The animals (n = 6/group, FB_1 vs. control, total n = 12) were fed Ssniff R/M-Z+H feed (Ssniff GmbH, Soest, Germany; Table 1). The Ssniff basic feed was ground on a 0.75-mm sieve size Retsch SR200 (Retsch GmbH, Haan, Germany) feed mill, and water and – only for the formula with added FB_1 – mycotoxin-containing fungal culture were added (the protocol is described below).

Table 1

Chemical and fatty acid composition of the diet

Chemical composition	
Dry matter (%)	88.4
Crude protein (%)	19
Crude fat (%)	3.5
Crude fibre (%)	3.6
Crude ash (%)	6.5
N-free extract (%)	55.9
Gross energy (MJ/kg)	16.4
Metabolisable energy (MJ/kg)	13.4
Fatty acid composition	**Weight %**
C14:0	0.01
C16:0	0.49
C16:1 n7	0.01
C18:0	0.08
C18:1 n9	0.65
C18:2 n6	1.9
C18:3 n3	0.25
C20:0	0.01
C20:1 n9	0.02

The mixture was homogenised, re-granulated and dried at 40 °C. The same preparation protocol was applied for the control animals but no fungal culture was mixed into their feed. The rats were kept in a 12-hour light and 12-hour dark daily rhythm, at 20 °C in a rodent room. The relative air humidity was 50%. Feed was offered *ad libitum*, and feed intake was measured daily. Water was offered *ad libitum*, and body weight was measured at the start and end of the study. After five days of feeding the experimental and control diets respectively, the rats were sacrificed by cervical dislocation and were immediately dissected. Total dissected fresh livers were weighed immediately and 0.5 g of the right lobe was

stored frozen (–80 °C) in Eppendorf tubes until analysis. Absolute weight was the fresh total liver weight; relative weight means the liver weight as a percentage of the total body mass. The kidney weight was also determined freshly. The experimental protocol was authorised by the Food Chain Safety and Animal Health Directorate of the Somogy County Agricultural Office, under the allowance number SOI/31/1679-11/2014.

Mycotoxin production

Fumonisin B_1 was produced by the application of *Fusarium verticillioides* strain MRC 826 according to the method of Fodor et al. (2008). The homogenised fungal culture contained FB_1 at a concentration of 3.44 g/kg. This fungal culture was mixed into the basal diet of the experimental animals, so as to provide feed contaminated with 50 mg/kg FB_1 toxin.

The mycotoxin concentration of the control and the experimental diet was determined by LC-MS (Shimadzu, Kyoto, Japan). The lower limit of detection (LOD) for FB_1 was 3 μg/kg. The diet fed to the control group did not contain detectable amounts of FB_1 (the complete absence of deoxynivalenol, zearalenone and T-2 toxin was as well controlled and confirmed).

Lipid analysis

Liver samples and the feed were homogenised (IKA T25 Digital Ultra Turrax, Staufen, Germany) in 20-fold volume of chloroform:methanol (2:1 v:v) and total lipid content was extracted according to Folch et al. (1957). Solvents were ultrapure-grade (Sigma-Aldrich, Schnelldorf, Germany) and 0.01% w:v butylated hydroxytoluene was added to prevent fatty acid oxidation. For the separation of lipid fractions, extracted total lipids were transferred to glass chromatographic columns, containing 300 mg silica gel (230–400 mesh) for 10 mg of total lipids (Leray et al., 1997). Neutral lipids were eluted with 10 mL chloroform for the above fat amount, then 15 mL acetone:methanol (9:1 v:v) was added, while 10 mL pure methanol eluted the total phospholipids. This latter fraction was evaporated under a nitrogen stream and was transmethylated with a base-catalysed $NaOCH_3$ method (Christie, 1982). Fatty acid methyl esters were extracted into 300 μL ultrapure n-hexane for gas chromatography, which was performed on a Shimadzu 2010 apparatus (AOC 20i automatic injector), equipped with a Phenomenex Zebron ZB-WAX Capillary GC column (30 m × 0.25 mm ID, 0.25 micrometer film, Phenomenex Inc., Torrance, CA, USA) and a flame ionisation detector (FID 2×10^{-11}). Characteristic operating conditions were: injector temperature: 270 °C, detector temperature: 300 °C, helium flow: 28 cm/sec. The oven temperature was graded: from 80 to 205 °C: 2.5 °C/min, 5 min at 205 °C, from 205 to 250 °C 10 °C/min and 5 min at 210 °C. The makeup gas was nitrogen. To identify individual FA, an authentic external FA standard (37 Compo-

nent FAME Mix, Sigma-Aldrich, Cat. No.: CRM47885) was used. Fatty acid results were expressed as weight % of total fatty acid methyl esters.

Analysis of lipid peroxidation

Lipid peroxidation (end-phase) was assessed by the determination of malondialdehyde (MDA) levels using the 2-thiobarbituric acid method (Placer et al., 1966). The concentration of reduced glutathione (GSH) was measured by photometry (Sedlak and Lindsay, 1968) and the activity of glutathione peroxidase (GPx) was determined according to Lawrence and Burk (1978). The concentration of conjugated dienes and trienes (initial phase lipid peroxidation) was determined by spectrophotometry (absorbance: 232 and 268 nm, respectively), using AOAC (1984) methods. All analyses were performed from liver tissue samples after storage at –80 °C.

Statistical analysis

For the comparison of group means (body weight, liver weight, feed intake), independent samples *t*-test was used with the SPSS 20 software (2012). Oxidation products, antioxidant parameters and FAs were compared by univariate ANOVA, and the model contained liver weight as a covariate.

Results

Body weight, liver weight, feed intake

At the beginning and at the end of the experiment the body weight was not different between the FB_1-intoxicated and the control groups (Table 2). The control group showed a slight (not significant) body weight gain, while FB_1 feeding compromised the growth of rats (the difference was not significant). When comparing the cumulative alterations during the five experimental days, significant difference was found in body weight gain between the FB_1-fed and the control groups. The liver weight and the relative liver weight showed a significant increase as a result of toxin feeding (FB_1 > control at day 5). No difference was found between the groups in kidney weight.

Feed intake tended to be lower in the group fed the FB_1-containing diet during the study, but the difference was significant only at days 3 and 4 (Fig. 1).

Fatty acid composition of hepatic phospholipids

Among the fatty acids determined (Table 3), the proportions of margaric acid (C17:0), α-linolenic acid (C18:3 n3), docosapentaenoic acid (C22:5 n3) and docosahexaenoic acid (C22:6 n3) were significantly higher than in the control

animals. This led to a significant decrease of the total n3 FA proportion and a concomitant increase of the n6/n3 ratio. Neither the number of double bonds in 100 acyl chains (unsaturation index, UI) nor the average fatty acyl chain length (ACL) was affected by the mycotoxin exposure.

Table 2

Somatic traits of the control and the fumonisin B_1-fed groups (n = 6 per group)

Somatic traits	Control group (mean ± SEM)	Fumonisin B_1 (mean ± SEM)	P (*t*-test)
Initial body weight, g	210.4 ± 12.4	242.3 ± 10.0	NS
Final body weight, g	217.3 ± 13.1	223.7 ± 23.0	NS
Liver, g	6.16 ± 0.30	7.50 ± 0.74	0.004
Kidneys, g	1.46 ± 0.15	1.67 ± 0.19	NS
Relative liver weight, %	2.85 ± 0.29	3.83 ± 0.45	0.049
Relative kidney weight, %	0.67 ± 0.10	0.75 ± 0.11	NS
Body weight gain, g	6.92 ± 2.55	–18.6 ± 24.8	0.05

NS = not significant

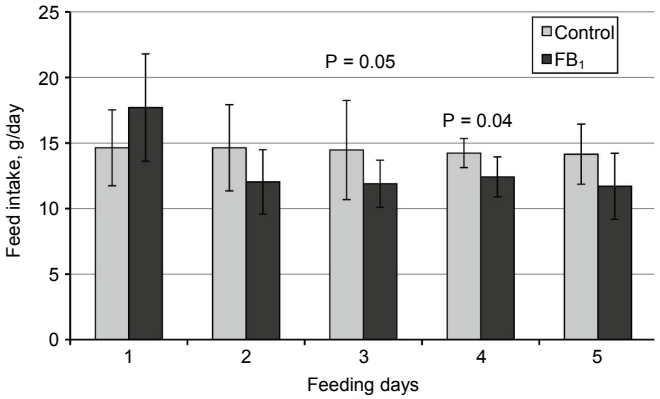

Fig. 1. Feed intake of the animals during the trial (g/day/animal)

Antioxidants and lipid peroxidation

Comparing the control and the FB_1-fed groups (Table 4) at the end of the study (day 5), the hepatic GSH concentration was lower and the tissue MDA concentration was higher in the FB_1-fed group, while the activity of GPx was not different. In contrast, FB_1-exposure significantly decreased the hepatic tissue concentration of conjugated dienes and conjugated trienes as compared to the control at the end of the experiment.

Table 3

Alterations caused by fumonisin B_1 feeding in the fatty acid composition of hepatic total phospholipids

Fatty acid composition of hepatic phospholipids	Control group (mean ± SEM)	Group fed fumonisin B_1 (mean ± SEM)	Difference P (ANOVA)
C14:0	0.21 ± 0.02	0.22 ± 0.09	NS
C15:0	0.21 ± 0.04	0.17 ± 0.06	NS
C16:0	16.3 ± 7.60	19.6 ± 3.68	NS
C16:1 n7	1.09 ± 0.15	0.97 ± 0.47	NS
C17:0	0.53 ± 0.10	0.41 ± 0.02	0.017
C18:0	19.1 ± 1.58	19.6 ± 2.85	NS
C18:1 n9	5.40 ± 0.76	4.39 ± 0.76	NS
C18:2 n6	14.2 ± 2.18	14.00 ± 1.55	NS
C18:3 n3	0.12 ± 0.01	0.10 ± 0.01	0.038
C20:1 n9	0.10 ± 0.03	0.10 ± 0.02	NS
C20:2 n6	0.53 ± 0.07	0.32 ± 0.20	NS
C20:3 n6	1.25 ± 0.15	0.91 ± 0.35	NS
C20:4 n6	31.4 ± 2.49	31.8 ± 1.84	NS
C22:5 n3	1.09 ± 0.20	0.75 ± 0.23	0.032
C22:6 n3	8.33 ± 0.75	6.67 ± 1.19	0.025
Σ saturated	36.5 ± 6.10	40.1 ± 1.70	NS
Σ unsaturated	63.5 ± 6.07	59.9 ± 1.74	NS
Σ monoenoic	6.56 ± 0.81	5.41 ± 1.20	NS
Σ polyenoic	57.0 ± 5.38	54.5 ± 2.17	NS
Σ n3	9.54 ± 0.92	7.52 ± 1.33	0.019
Σ n6	47.4 ± 4.72	47.0 ± 1.09	NS
Σ n6 / Σ n3	4.99 ± 0.40	6.43 ± 1.28	0.039
UI	220.8 ± 19.2	207.4 ± 12.8	NS
ACL	18.66 ± 0.23	18.52 ± 0.17	NS

NS = not significant; UI = unsaturation index; ACL = average fatty acyl chain length

Table 4

Hepatic antioxidant and oxidation parameters of the control and the toxin-fed rats

Hepatic antioxidant parameters	Control group (mean ± SEM)	Group fed fumonisin B_1 (mean ± SEM)	Difference* P (ANOVA)
GSH (micromoles/g protein)	3.90 ± 0.26	3.76 ± 0.12	0.045
GPX (IU/g protein)	2.97 ± 0.32	2.87 ± 0.09	NS
MDA (micromoles/g)	15.4 ± 1.66	18.71 ± 1.37	0.06
Conjugated dienes (ABS 232 nm)	0.25 ± 0.005	0.22 ± 0.004	0.007
Conjugated trienes (ABS 268 nm)	0.12 ± 0.003	0.11 ± 0.002	0.008

*Significance of differences between the control and the FB_1 groups at the end of the trial; NS = not significant

Discussion

Body weight, liver weight, feed intake

The first notable hint that FB_1 depresses growth in rats was published by Gelderblom et al. (1994), who applied a longer (21-day) setting with the lowest FB_1 concentration of 250 mg/kg feed. According to these authors, feed refusal is provoked by FB_1 within the first 14 feeding days and this effect is diminished later on (in the last 7 days).

Concerning liver weight, Gelderblom et al. (1994) reported that FB_1 effectively delays hepatocyte proliferation in two feeding regimes: 250 mg FB_1/kg feed for 21 days and even by a single gavage dose of 5 mg FB_1/100 g body weight. In contrast, Abel and Gelderblom (1998) showed that FB_1 contaminations at doses of 10, 50 and 100 mg/kg feed for 21 days, respectively, did not adversely affect the body weight gain and the relative liver weight; this effect was only found at doses of 250 and 500 mg/kg feed.

Abel and Gelderblom (1998) found a lowered feed intake only at an FB_1 concentration of 250 mg/kg feed, and in the 21-day study the feed intake reached the control level after 14 days. It is thus a new finding of the present study that even an FB_1 dose of 50 mg/kg feed has an adverse effect on the feed intake, and this occurs as early as three days after toxin administration.

Fatty acid composition of hepatic phospholipids

The FA composition analysis of hepatic total phospholipids was invented to provide novel data on the acute membrane-damaging effect of FB_1. The presence of margaric acid (C17:0) is bound to microbial activity, since vertebrates do not synthesise odd-chain FAs (Leray, 2013). As rats perform coprophagy, they ingest bacterial fatty acids which are then incorporated into their glycerolipids. It is important to note that in rabbits (performing caecotrophy) the red cell membrane (Szabó et al., 2014) and the hepatic mitochondrial membrane (Szabó et al., 2016) showed identical changes as a result of 10 mg/kg feed FB_1 exposure for 28 days. It might be thus assumed that in rodents the lowered cell membrane margaric acid proportion (induced by FB_1 toxin exposure) contributed to the increase of membrane fluidity, as a means of counterbalancing the proportional decrease of the much more fluid polyunsaturated FAs (C22 PUFAs).

The decrease of the C22 penta- and hexaenoic acids was preceded by a slight proportional decrease of their precursor, α-linolenic acid. Although α-linolenic acid was present in the diets as a minor component, its elongated and poly-desaturated products were not, as the Ssniff diet brand used in the study does not contain any animal by-products or traces thereof (Table 1). The reason why C22 n3 PUFA underwent a proportional decrease might be partly their very high sensitivity towards lipid peroxidation (as reflected by MDA and in particu-

lar by GSH). The relative susceptibility difference between C18:3 n3 and C22:6 n3 is approximately 4-fold (Hulbert, 2005). It may thus be a direct consequence of oxidative stress and membrane lipid damage that the peroxidation products of lipids (MDA) were indeed detected in the whole-tissue samples (Table 4). Gelderblom et al. (1997) reported detailed results on FB_1-induced alterations of non-ceramide, polar lipids in the rat liver. The trial settings were different from ours, namely 1–10–20 mg/kg feed for two years and 50–100–250 mg/kg feed for 21 days, respectively. In those trials the FA profile of the PC and PE fractions was determined, while in our analysis these were not handled separately. Anyhow, the alterations detected were of similar nature. Gelderblom et al. (1997) reported a characteristic n6 (C18:2 n6) FA proportional increase in the PE fraction at FB_1 doses of 100 and 250 mg/kg feed. Lower toxin concentration but prolonged exposure induced identical alterations in the total FAs of the liver. According to Gelderblom et al. (1997), there is a shift within the n6 FA group (↑ C18:2 n6 and ↓C22:5 n6), not via the reduction of the n3 FAs, but due to the disturbance of the Δ6 desaturase activity. Our study demonstrated the same phenomenon, since Δ6 desaturation is an essential step (besides elongation and Δ5 desaturation) in the metabolism (formation) of C22 PUFA in both groups. The authors furthermore reported decreased C20:4 n6 (arachidonic acid) levels in the plasma in both studies, though the formation of eicosanoids was not analysed. It is important that the disruption of PUFA (mostly n6) was attained at the 250 mg/kg feed dosage, while the lower dose applied in our trial led to a similar effect in the n3 FA group of profound oxidative sensitivity. Gelderblom et al. (1997) defined this effect as a part of the acute effect of FB_1; in the longer-term treatment this oxidative effect was not proved and, in addition, the n3 FA proportion increased in the PE and PC fractions. The authors draw the conclusion that the potentially emerging eicosanoids might have been the compounds that retarded cell growth (lower relative liver weight). Not rejecting this hypothesis, the present dataset adds confirmative information that the hepatocellular antioxidant defence system may also play a compensatory role against entering the propagation phase of lipid peroxidation. This is supported by the production of conjugated dienes and conjugated trienes, which are formed mostly during the initiation phase of lipid peroxidation (Halliwell and Cross, 1994).

Reduced glutathione and glutathione peroxidase

Reduced glutathione is a well-known marker of cell antioxidative capacity used in toxicological studies as well (Klaric et al., 2007). Hepatic GSH level was slightly lowered by FB_1 in our study. Numerous published studies confirm that FB_1 exposure effectively lowers plasma or whole liver GSH concentration, but one of the most targeted studies pointed out that this decrease is ultimately the result of oxidative stress associated free radical scavenging (Stockmann-Juvala et al., 2004). According to the authors, FB_1 may act as a cell membrane structure

modifying compound, altering the membrane lipid profile (see the section *Fatty acid composition of hepatic phospholipids*) and thus contributing to hydrogen peroxide production. Although FB_1 is primarily a ceramide synthesis inhibitor (Dutton, 1996), it is well known that, as a secondary effect, FB_1 effectively modifies hepatic PL composition in rats (Gelderblom et al., 1997). The fatty acid profile of the lipid fractions analysed was enriched in n6 FAs in the long-term study, showing a compensatory effect against augmented lipid oxidation.

Glutathione functions as an electron donor; it is easily reduced, which form is then rapidly converted to glutathione disulphide by glutathione reductase. In our study the activity of this enzyme was not determined, but that of another antioxidant enzyme, glutathione peroxidase (GPx) was. According to Kang and Alexander (1996), kidney cells do not react to FB_1 with a GPx activity alteration *in vitro*, but Marnewick et al. (2009) reported increased GPx activity induced by an FB_1 dose of 250 mg/kg feed for 21 days in rats. Our short and not drastically high exposure did not affect the hepatic tissue activity of GPx.

Based on the above information it seems that a short-time and relatively low-dose FB_1 exposure does not evoke enzymatic antioxidant defence (GPx) but influences non-enzymatic (GSH) antioxidant activity, most probably via the augmented production of lipid-derived oxidation products (MDA).

Conjugated dienes and conjugated trienes

During the formation of hydroperoxides from PUFA, conjugated dienes (CD) and conjugated trienes (CT) are typically produced, due to the rearrangement (virtually migration) of the double bonds, which are naturally allocated in a methylene-group interrupted form. The resulting CDs absorb at 234 nm, while CTs at 268 nm. Conjugated dienes are more stable than non-conjugated dienes due to factors such as delocalisation of charge through resonance and hybridisation energy (Mead et al., 1986).

The finding that in our study CD and CT production was diminished by FB_1 might be explained by two factors: (1) the proportion of their precursor FAs was lower in the FB_1-intoxicated animals, and (2) in the hepatocellular plasma the concentration of endogenously synthesised antioxidants (primarily GSH) was rather high (5–10 mM), and these compounds were readily present to inhibit the propagation of lipid peroxidation. As far as the authors are aware, there are two reports characterising the augmented initiation phase of lipid peroxidation by means of CDs and CTs (Szabó-Fodor et al., 2015; Bócsai et al., 2016), but as an effect of T-2 and deoxynivalenol + zearalenone toxins, respectively. For fumonisin B_1 this is the first report analysing the initial phase of lipid peroxidation, which was in fact effectively compensated for by the endogenous GSH and the relative substrate shortage.

Malondialdehyde

Malondialdehyde is a product of methyl-fatty acids, formed via an intermediate step as prostaglandin-like endoperoxide (Pryor and Stanley, 1975). It is produced from PUFA with at least two methylene-interrupted double bonds, and once emerging, it is present as a less reactive (but mostly towards DNA) enolate anion, exerting genotoxic effects. Malondialdehyde is known to crosslink and polymerise membrane components and to react with nitrogenated DNA bases to form common adducts (Abel and Gelderblom, 1998). Abel and Gelderblom (1998) reported *in vitro* results on primary rat hepatocytes, namely FB_1-induced MDA production. Sahu et al. (1998) reported elevated MDA production *in vitro* as a result of FB_1, originating from the nucleolemmal lipid peroxidation and augmenting DNA damage. However, Domijan et al. (2008) showed that low, single-dose treatment with FB_1 (5, 50 and 500 μg/kg body weight) did not induce oxidative stress, while markedly damaged liver cell DNA was found. In our study a slight increase was found, meeting a less strict significance level. The reason for this might be that the production of MDA depends on its precursors (primarily n3 PUFA), most of which were decreased (Table 3) and have profound and specific oxidative sensitivity (Tirosh et al., 2015). However, MDA is not only cytotoxic but also indicative of the end-phase of lipid peroxidation and a pathological state (Del Rio et al., 2005).

Conclusions

Testing the acute effects of a naturally occurring fumonisin B_1 dose (50 mg/kg feed), in a rather short exposure period, decrease of mostly elongated, n3 polyunsaturated fatty acids was found in the hepatic total phospholipids of rats. This fatty acid profile modification effect was partly compensated for by the endogenous glutathione (preventing the production of conjugated dienes and trienes, as initial phase of lipid peroxidation products), meanwhile enzymatic antioxidant defence system (glutathione peroxidase) was not activated.

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