

IMPACTS OF MICROCYSTIN, A CYANOBACTERIAL TOXIN, ON LABORATORY RODENTS *IN VIVO*

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Received: May 6, 2008

Abstract

ZIKOVÁ, A., KOPP, R.: *Impacts of microcystin, a cyanobacterial toxin, on laboratory rodents in vivo*. Acta univ. agric. et silvic. Mendel. Brun., 2008, LVI, No. 5, pp. 263–274

Cyanobacterial water blooms became a global problem/issue because beside a dramatic deterioration of water quality parameters they also produce cyanobacterial toxins being harmful for animals and humans. Cyanotoxins especially the most prominent one, microcystin-LR (MC-LR), are of major concern and they have been reported to cause even death of mammals following ingestion or ingurgitation due to hepatotoxic modes of action. The aim of the recent study is to summarize briefly the impacts of microcystin on laboratory rodents, mice and rats, being used as models for other mammals including human beings. Most experimental approaches used intraperitoneal rather than oral and intratracheal application of microcystins, especially MC-LR, being the most efficient way to induce adverse impacts on different target organs. However, no matter how the exposure of rodents was performed, microcystins induced severe harmful impacts on the different target organs, preferentially the liver, for instances hemorrhages and apoptosis in liver, liver tumours, adverse effects on gut, kidney, testis and epididymis including spermatogenesis, on lung, on serum parameters and on progeny. In addition to these histological findings, microcystin was found to affect specifically biochemical parameters of target organs such as enzymes e.g. GST, CAT, GR, GPX, SOD, AST, ALT, γ -GT, protein phosphatases, SDH, SoDH and LDH or stress proteins such as HSP-70 and further parameters such as hepatic sulfhydryl content, GSH depletion, total bilirubin, urea nitrogen, and creatinine. Gene array analyses revealed that microcystin affects genes related to actin organization, cell cycle, apoptosis, cellular redox potential, cell signalling, albumin metabolism, glucose homeostasis pathway and organic anion transport polypeptide system. In combination with a further proteomics approach the proteomic analyses indicate that liver apoptosis induced by microcystin can be induced by two pathways: the BID-BAX-BCL2 and the reactive oxygen species pathway. The reviewed data clearly show that microcystin, especially MC-LR is able to cause severe adverse impacts on laboratory rodents and therefore there is an emerging need for further research to cover the major concern about cyanobacterial water blooms affecting mammals including human beings.

microcystin; mice; rats; intraperitoneal, oral, intratracheal application

ALT = alanine amino transferase, AST = aspartate aminotransferase, CAT = catalase,

GPX = glutathione peroxidase, GR = glutathione reductase, GSH = glutathione synthetase,

GST = glutathione-S-transferase, HSP-70 = heat shock protein 70, LDH = lactate dehydrogenase, SDH = succinate dehydrogenase, SOD = superoxide dismutase,

SoDH = sorbitol dehydrogenase, γ -GT = γ -glutamyl transpeptidase

INTRODUCTION

Since several years the occurrence of water blooms caused by mass development of cyanobacteria in fresh and in sea water has become an important issue concerning environmental research (Carmichael, 1989; Demir, 2007; Fonseca and Bicudo, 2008). The biomass production of cyanobacteria is related to massive input of nutrients especially of nitrogen and phosphorus into water bodies by human activities such as agricultural fertilization and sewage effluents and, in addition, the higher mean temperature caused by cli-

mate change. Besides negative effects such as deterioration of physicochemical parameters of water environment (oxygen depletion and bad odour from decaying cyanobacterial biomass), cyanobacteria are able to produce a wide range of bioactive compounds (Carmichael, 2001). These substances are called cyanotoxins and can be classified into three groups concerning their structure: cyclic peptides (e.g. microcystins, nodularins), alkaloids (e.g. anatoxins, saxitoxins) and lipopolysaccharides that are produced by all cyanobacterial species (Sivonen and Jones, 1999). Cyanotoxins have severe effects on vertebrates due to their chemical structures. Cyclic peptides are mainly associated with hepatotoxicity whereas alkaloids are known to be neurotoxic and lipopolysaccharides have the potential to be irritants. Microcystins, the most common cyanotoxins in freshwaters, are a family of toxins produced by species primarily *Microcystis aeruginosa* but also by other *Microcystis* species and other genera, namely *Anabaena*, *Oscillatoria* and *Nostoc* (Dawson, 1998). By far the main occurring microcystin is microcystin-LR, a hepatotoxin being a threat to health of other animals and even humans. There have been reports of several cases of acute animal poisoning episodes (Done and Bain, 1993; Fitzgerald and Popenga, 1993; Carbis et al., 1994; Van Halderen et al., 1995; Frazier, 1998; Boaru et al., 2006). The microcystins have been also associated with human toxicity. Exposure to these cyanotoxins resulted in acute sickness and death in dialysis patients in Brazil (Jochimsen et al., 1998) and it has been suggested that microcystins may play a role in the high incidence of hepatocellular carcinoma present in specific regions of China (Yu, 1995). Many investigations of microcystins revealed that they cause severe hepatotoxic effects in diverse mammalian species (Hermansky et al., 1993; Chernoff et al., 2002; Weng et al., 2007; Ito et al., 1997; Nishawaki-Matsushima et al., 1992). Various ways of exposure are applied in order to test the toxicity of microcystin-LR in mammals including intraperitoneal, oral and intratracheal application. The aim of this article is to summarize and review the impacts of microcystins, mainly of microcystin-LR (MC-LR) on rodents, used as models for mammals including human beings, considering toxicity related to different exposure routes (cf. Tab. I-III).

DISCUSSION AND CONCLUSIONS

MC-LR is the most common cyanotoxin known to be hepatotoxic in mammals; however, summarized data presented in Tab. I-III demonstrate besides its hepatotoxicity several further adverse biological impacts on various target organs. Laboratory rodents are generally accepted as good models for mammalian toxicology including humans. Because of several severe impacts of cyanotoxins on mammals (Done and Bain, 1993; Frazier, 1998; Fitzgerald and Popenga, 1993; Carbis et al., 1994; Van Halderen et al., 1995) including humans (Jochimsen et al., 1998; Yu, 1995) many investigations were undertaken in order to elucidate the potential impacts of microcystins, espe-

cially MC-LR or cyanobacterial extracts and scums using different experimental approaches dealing with various exposure routes. The most common exposure pathways for microcystin application are: intraperitoneal injection (cf. Tab. I), oral administration (cf. Tab. II) and intratracheal application (cf. Tab. III). Results from different studies presented in Tab. I-III clearly demonstrated that intraperitoneal injection caused most efficiently adverse impact of MC-LR on various target organs, preferentially the liver, for instances hemorrhages and apoptosis in liver and liver tumours. Adverse histological effects were also detected in gut, kidney, testis and epididymis including spermatogenesis, as well as in lung, in serum parameters and in same target organs of progeny. Besides these histological findings biochemical evaluation of various parameters in target organs were determined. Adversely affected were enzymes such as GST, CAT, GR, GPX, SOD, AST, ALT, γ -GT, protein phosphatases, SDH, SoDH and LDH, and the stress protein HSP-70. In addition, further parameters such as hepatic sulfhydryl content, GSH depletion, total bilirubin, urea nitrogen, and creatinine became negatively influenced. More recently, gene array analyses revealed that MC-LR affects genes related to actin organization, cell cycle, apoptosis, cellular redox potential, cell signalling, albumin metabolism, glucose homeostasis pathway and organic anion transport polypeptide system (Chen et al., 2005). In combination with an advanced proteomics approach (Weng et al., 2007) the proteomic analyses indicate that liver apoptosis induced by MC-LR can be induced by two pathways: the BID-BAX-BCL2 and the reactive oxygen species pathway.

Comparison of different experimental approaches concerning various MC-LR applications revealed that intraperitoneal injection is the most efficient way to induce adverse impacts. However, natural exposure routes of MC-LR in mammals are rather due only to oral or tracheal ingestion. Recent results concerning oral (cf. Tab. II) and tracheal ingestion (cf. Tab. III) confirmed that much higher concentrations of microcystins are needed to evoke similar adverse effects compared to intraperitoneal injection. However, different exposure routes are causing different impacts on target organs as seen by oral administration of microcystins affecting primarily gastrointestinal tract. Inhalation or tracheal ingestion demonstrated severe impacts on inhalation tract (cf. Tab. III). Therefore because of different exposure routes causing different impacts on target organisms more emphasis should be taken to investigate the effects of natural exposure routes such as oral, tracheal, and even transdermal ones instead of testing intraperitoneal application, that is not happening under natural conditions.

Results of the various exposures are presented in detail by Tab. I-III.

Tab. I consists of data obtained by intraperitoneal injections. Tab. II shows the results from oral administration of MC-LR and Tab. III represents findings from intratracheal application, inhalation and tail vein injection of MC-LR.

1: *Intraperitoneal injection*

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
Balb/c mice	♀, 7 weeks	75% LD ₅₀ pure MC-LR	8, 16, 24, 32 h pe	liver-detoxification of MC-LR by increase in GST activity, synthesis of GSH, GPX.	Gehring et al. (2004)
Swiss mice	♂, 4 and 12 weeks	48.2 µg.kg ⁻¹	2, 8 h, 1, 2, 3, 4 d pe sublethal dose of MCs	lungs-increase of alveolar collaps and polymorphonuclear cells due to lesion time, maximum value reached earlier in young animals.	Picanoço et al. (2004)
Balb/c mice	♀, 6 and 9 weeks	40, 48, 57.6, 60 µg.kg ⁻¹ pure MC-LR	24 h experiment 4, 7, 11, 17, 21 h pe	liver-hemorrhage within 7 h, paracentral necrosis, apoptosis in the centrilobular and midlobular regions.	Yoshida et al. (2001)
Kunming mice	pregnant ♀, 23-28g	3, 6, 12 µg.kg ⁻¹ cell extract of <i>M. aeruginosa</i>	18 d experiment from gestational days 6-15 daily	decrease in body weight gain of pregnant mice (12 µg.kg ⁻¹), fetuses-decreased body weight, body length, tail length (12 µg.kg ⁻¹), fetuses liver- petechial hemorrhage, hydropic degeneration (6, 12 µg.kg ⁻¹).	Bu et al. (2006)
KM mice	♂, 25-30g, 8 weeks	3.33, 6.67 µg.kg ⁻¹ cell extract of <i>M. aeruginosa</i>	14 d, daily 8 h pe	decrease of mean body weight, mean absolute weight of the testes and epididymis, increased relative mean weight of the testes, damaged testes-more pronounced space between the seminiferous tubules, decreased sperm quality, reduced sperm motility and viability.	Ding et al. (2006)
Wistar rats	♂, about 200g	100 µg.kg ⁻¹ pure MC-LR		liver-increased weight, higher specific activity of sucrose, lactase and ALP not modified; ACP, SDH, lysosomal and mitochondrial membrane markers were increased, increased peroxidative status in serum and intestinal mucosa.	Moreno et al. (2003)
mice		101 µg.kg ⁻¹ [³ H]-MC-LR	death, 6 h pe	liver contained 56 ± 1 %, intestine 7 ± 1 %, kidney 0.9 ± 0.2 %, carcass 10 ± 1 % of injected dose; heart, spleen, lung and skeletal muscle contained < 1 % of [³ H]-MC-LR.	Robinson et al. (1989)
Balb/c mice	♂, adult, 20-22g	100 µg.kg ⁻¹ lethal 12, 23, 45 µg.kg ⁻¹ sublethal dose of MC-LR		hepatic nuclear extract-inhibition of nuclear protein phosphatase activity within lethal dosing.	Guzman et al. (2003)
Balb/c mice	♀, 7 weeks	75% LD ₅₀ MC-LR	8, 16, 24, 32 h pe	GIT – duodenum-the most significant increase in apoptotic index, followed by jejunum and ileum; increase of apoptoses index in time.	Botha et al. (2004)

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
Swiss albino mice	♀, 24-26 g	38.31 µg.kg ⁻¹ MC-LR 76.62 µg.kg ⁻¹ MC-LR	15, 30, 60 min, and 1, 2, 3 d pe	no effect of other antioxidant enzymes except CAT and GR at 38.31 µg.kg ⁻¹ . Time-dependent increase in HSP-70 expression; Liver body weight index, hepatic lipid peroxidation and GSH depletion increase. Decrease in the activity of GPX, SOD, CAT, GR, GST.	Jayaraj et al. (2006)
Swiss mice	♂, 25-30 g, 6-8 weeks	40 µg.kg ⁻¹ MC-LR	2, 8 h, 1, 2, 4 d pe	no MC or inhibition of PPases detected in mice lungs. Rapid increase in lung impedance and an inflammatory response with interstitial edema and inflammatory cell recruitment.	Soares et al. (2007)
Swiss albino mice	♀, 24-26 g	43 µg.kg ⁻¹ MC-LR	30 min pe and MDT	significant increase in liver body weight index, increase in serum levels of hepatic enzymes (AST, ALT and γ-GT), enhanced LDH leakage, DNA fragmentation, depletion of hepatic glutathione. liver histology-time dependent pathological lesions like congestion, hemorrhage, portal mononuclear cell infiltration and obliteration of chromatin material. Lung lesions in bronchi and parenchyma.	Gupta et al. (2003)
Rats	fed	LD ₅₀ (122 µg.kg ⁻¹) 100, 150, 200 µg.kg ⁻¹	MDT: 11.2, 18.2, 31.9 h	increase in liver weight and serum levels of SoDH, plasma membranes isolated from liver exhibited toxin-induced cytoskeletal elements changes.	Miura et al. (1991)
Rats	fasted	LD ₅₀ (72 µg.kg ⁻¹) 100, 150, 200 µg.kg ⁻¹	MDT: 1.8, 1.7, 1.5 h	increase in liver weight and serum levels of SoDH; plasma membranes isolated from liver exhibited toxin-induced cytoskeletal elements changes. Complete inhibition of state 3 respiration in liver mitochondria.	Miura et al. (1991)
Wild type mice B6.129- <i>Trp53</i> ^{+/+} N5 mice		40 µg.kg ⁻¹ MC-LR	daily for 28 d 4, 24 h, 4, 14, 28 d after	increase in plasma hepatic enzyme activities, decrease in total protein, first dose albumin and glucose concentration. Gene array analysis revealed in the actin organization, cell cycle, apoptotic, cellular redox, cell signalling, albumin metabolism, glucose homeostasis pathway, and the organic anion transport polypeptide system.	Clark et al. (2007)

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
Swiss albino mice	6 weeks (24-26 g) 12 weeks (31-34 g) 18 weeks (34-38 g) 24 weeks (37-42 g) 30 weeks (42-45 g) 36 weeks (43-46 g)	LD ₅₀ (43 µg.kg ⁻¹)	24h	time to death in toxin treated animals decreased with age of mice; significant increase in liver body mass index and increases in serum enzymes (LDH, AST, ALT, γ-GT, SoDH)	Rao et al. (2005)
NIH non-Swiss mice	♀, 20-24 g	12.5, 25, 50, 100 µg.kg ⁻¹ MC-LR	15, 30, 45, 60 min, 2h pe	liver weight increased, 50 and 100 µg.kg ⁻¹ Kupffer cell hyperplasia, loss of hepatic architecture and necrosis. Serum enzymes increased (LDH, ALT, AST). Hepatic sulphydryl content decreased. 100 µg.kg ⁻¹ lethal dose.	Hermansky et al. (1990)
Balb/c mice	♀, adults	100 µg.kg ⁻¹ MC-LR	15, 30, 60, 90 min pe	liver lesions, higher liver weight, necrosis, diasciation and rounding of centrilobular hepatocytes. Kidney weight increased and vacuolization of proximal tubular epithelium with tubular dilatation, increase of ALT, ALP, total bilirubin, urea nitrogen, creatinine, 100 µg.kg ⁻¹ lethal dose	Hooser et al. (1989)
Sprague-Dawley rats	♀; ♂; 175-200 g	20-1,200 µg.kg ⁻¹ MC-LR	5-60 min, 3-24h	liver lesions, higher liver weight, necrosis, diasciation and rounding of centrilobular hepatocytes. Kidney weight increased and vacuolization of proximal tubular epithelium with tubular dilatation, increase of ALT, ALP, total bilirubin, urea nitrogen, creatinine, 160 µg.kg ⁻¹ lethal dose.	Hooser et al. (1989)
CD-1 mice	♀ pregnant	2-160 µg.kg ⁻¹	during gestation days 7-8, 9-10, or 11-12 sampling at d 17	lethality at 128 and 160 µg.kg ⁻¹ , liver necrosis with hemorrhage, fetuses were not affected by teratogenicity	Chernoff et al. (2002)
Balb/c mice	♂, 20-35 g	20-40 µg.kg ⁻¹	24h	lethality of 25, 32.5, and 40 µg.kg ⁻¹ was 0, 50, and 100% increase in weight of liver and kidney hepatic hemorrhage	Lovell et al. (1989)
Swiss Webster mice	♂, 6 weeks, 22-28 g	1 st 55 µg.kg ⁻¹ MC-LR 2 nd 75 µg.kg ⁻¹	1 st sublethal dose 2 nd LD 2 or 3 d later	after priming by sublethal dose LD caused increased survivorship causing weakness, recumbency, anorexia, icterus, and gross liver lesions	Lovell et al. (1989)

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
Ballb/c mice	♀, 16-20 g	50, 60, 70 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	24h	liver- transcriptomics: affecting 61 genes related to apoptosis; proteomics: 35 proteins were up and 30 down regulated; computer simulation of data revealed that 50 $\mu\text{g}\cdot\text{kg}^{-1}$ caused apoptosis mainly by BID-BAX-BCL2-pathway; 70 $\mu\text{g}\cdot\text{kg}^{-1}$ impacted apoptosis mainly by ROS pathway	Chen et al. (2005)
NIH non-Swiss mice	♀, 22-24 g	100 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	15-60 min	liver-hepatocyte distortion, mitochondrial aggregation, accumulation of endoplasmic reticulum, no damage of sinusoidal endothelial cells	Hermansky et al. (1993)
ICR mice	♂, 20-27 g	35 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	1-45 min, 1-24h	MC-LR appeared in serum and liver after 15 min and was present up to 24 h, hepatic protein phosphatase 2A decreased after 1-2h	Lin & Chu (1994)
Fisher 344 rats	♂, 7 weeks	priming by diethylnitrosamine 1, 10 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	twice per week over weeks 2-8	liver-tumor promoting, GST foci increased, inhibition of protein phosphatase type 1 and 2A	Nishiwaki-Matsushima et al. (1992)
ICR mice	♀, 14 weeks	[³ H]-dihydro-MC-LR	5, 15, 30, 60 min	distribution of [³ H]-dihydro-MC-LR preferentially in liver (71.5% after 1h) all other organs less than 1.4%	Nishiwaki et al. (1994)
Ballb/c mice	20g	45 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	2-24 h	liver-hepatocellular hypertrophy, loss of vacuolation, glycogen depletion, apoptosis	Guzman & Solter (2002)
Cr1:CD-1 (ICR)BR mice	♀, ♂	50, 158, 500 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	up to 14 d	LD 50 between 50 and 158 $\mu\text{g}\cdot\text{kg}^{-1}$; liver hemorrhage, pallor of kidney, spleen, and adrenal	Fawell et al. (1999)
ICR mice	♂, 8 weeks	60 $\mu\text{g}\cdot\text{kg}^{-1}$ MC-LR	12h pe	large amount of ROS generation in mice liver, upregulated the expression of BAX and BID, caused the mitochondrial membrane protein loss and hepatocyte apoptosis as well as liver injury	Weng et al. (2007)

II: Oral administration of MC-LR

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
CrI:CD-1 (ICR)BR mice	♀, ♂	500; 1,580; 5,000 µg.kg ⁻¹ MC-LR	single dose up to 14 d daily	LD 50 at 5,000 µg.kg ⁻¹ , liver hemorrhage, necrosis, vacuolation	Fawell et al. (1999)
CrI:CD-1 (SD)BR rats	♀, ♂	500; 1,580; 5,000 µg.kg ⁻¹ MC-LR	single dose up to 14 d daily	not lethal, liver hemorrhage, necrosis, vacuolation	Fawell et al. (1999)
CrI:CD-1 (ICR)BR mice	♀, pregnant	200; 600; 2,000 µg.kg ⁻¹ MC-LR	during gestation d 6-15 daily	not lethal, liver hemorrhage, necrosis, vacuolation, 2,000 µg.kg ⁻¹ caused developmental toxicity on progeny	Fawell et al. (1999)
Balb/c mice	♀, 6 weeks	20 µg.l ⁻¹ MC-LR in drinking water	3-18 months	calculated intake ca. 35 µg/mouse, no toxic effect by chronic exposure to MC-LR	Ueno et al. (1999)
Mice	25 g	<i>M. aeruginosa</i> in drinking water a.l. or in scum 15,000 cells ml ⁻¹		scum containing <i>M. aeruginosa</i> was preferentially chosen for drinking and caused lethality of 50% and 100% after 48h and 6 d, respectively	Rodas & Costas (1999)
ICR mice	♀, 8 weeks	[³ H]-dihydro-MC-LR	3, 6, 19h, 3, 6 d	distribution of [³ H]-dihydro-MC-LR preferentially in GIT (37.6% after 19h) but only 0.68% in liver	Nishiwaki et al. (1994)
Balb/c mice ICR mice		500 µg.kg ⁻¹ MC-LR	0, 1, 6, 7, 12, 13 weeks	Balb/c mice had lethality > 50%, ICR mice nearly no lethality	Ito et al. (2000)
Swiss albino mice	6 weeks (24-26 g), 36 weeks (43-46g)	3.5 g MCE.kg ⁻¹ (LD50)	24h	similar to i.p. administration, time to death in toxin treated animals decreased with age of mice, glutathione depletion and increases of hepatic lipid peroxidation, DNA fragmentation, liver mass index, and serum enzymes (LDH, AST, ALT, γ-GT, SoDH)	Rao et al. (2005)
Balb/c mice	♀, 6 weeks	8-20 mg.kg ⁻¹ MC-LR	single dose	medial lethal dose was 10.9 mg.kg ⁻¹ . Hepatoceellular injuries with hemorrhage and necrosis. Apoptotic cell death of hepatocytes. Lethality of MC-LR much lower in oral dosage than by i.p. administration but toxic effects are similar.	Yoshida et al. (1997)
ICR mice	♂, 32 weeks, 48.2±3.8g 5 weeks, 27.4±1.2g	500 µg.kg ⁻¹ MC-LR	2, 5 19h pc gastric intubation	aged mice (32 weeks) changes in the liver, rough surface of the stomach, small intestinal mucosa. Liver changes were not found in young mice (5 weeks). Hepatotoxicity by oral administration of MC-LR is deeply related to aging, and particularly to conditions in the small intestine such as permeability of capillaries in the villi	Ito et al. (1997)

III: Intratracheal and tail vein administration, inhalation exposure

Experiment. Animals	Sex, weight, age	Exposure concentr.	Exposure time	Observed effects	Reference
ICR mice	♂, 5 weeks, 27.6±1.3 g	intratracheal admin. 50-200 µg.kg ⁻¹ MC-LR	until death	MC-LR accumulation caused bleeding in liver	Ito et al. (2001)
ICR mice	♂, 5 weeks, 27.6±1.3 g	intratracheal admin. LD (100 µg.kg ⁻¹ MC-LR)	5, 10, 20, 30, 45, 60, 90, 120 min	MC-LR accumulation caused bleeding in liver after 90 min.	Ito et al. (2001)
ICR mice	♂, 5 weeks, 27.6±1.3 g	intratracheal admin. sublethal (50 µg.kg ⁻¹ MC-LR)	7, 24, 48 h, 3, 4, 7, 10, 14 d	after 2 weeks, small amounts of MC-LR were still present in epithelial cells in the gastrointestinal mucosa	Ito et al. (2001)
Balb/c mice	♂, 6-8 weeks	inhalation exposure 260-265 MC-LR.m ⁻³	7 d 0.5, 1 and 2 h	microscopic lesions in the nasal cavity of mid- and high-dose groups, necrosis of respiratory epithelium, neutrophilic inflammation, degeneration, necrosis and atrophy of the olfactory epithelium, no-adverse-effect dose 3 µg.kg ⁻¹ b.w.≈20 ng.cm ⁻² nasal epithelium.	Benson et al. (2005)
VAF/pplus CD-1 Mice	♂, 20-27 g	i.v. via tail vein 35 µg.kg ⁻¹ [³ H]-MC-LR	6, 12 h, 1, 2, 3, 4, 5, 6 d pe	at 60 min, liver contained urine, feces contained 67±4% of dose, during 6 days no change, 23.7±1.7% of dose was excreted (9.2±1.0% in urine, 14.5±1.1% in feces)	Robinson et al. (1991)

a.l. = ad libitum, ACP = acid phosphatase, ALP = alkaline phosphatase, ALT = alanine amino transferase, AST = aspartate aminotransferase, CAT = catalase, GIT = gastrointestinal tract, GPX = glutathione peroxidase, GR = glutathione reductase, GSH = glutathione synthetase, GST = glutathione-S-transferase, HSP-70 = heat shock protein 70, LDH = lactate dehydrogenase, MCE = microcystin extract, MDT = mean time to death, pe = post exposure, ROS = reactive oxygen species, SDH = succinate dehydrogenase, SOD = superoxide dismutase, SoDH = sorbitol dehydrogenase, γ -GT = γ -glutamyl transpeptidase

SOUHRN

Vliv microcystinu, toxinu sinic, na laboratorní hlodavce *in vivo*

Sezonní výskyt vodních květů sinic se v poslední době stal celosvětově diskutovaným tématem a to nejen díky zhoršení hydrochemických parametrů vodního prostředí v důsledku rozkladu biomasy, ale také v souvislosti s produkcí cyanotoxinů, které jsou nebezpečné pro zvířata i lidi. Je dokonce zaznamenáno několik případů úmrtí savců v důsledku požití cyanotoxinů, zejména nejběžnější se vyskytujícího toxinu, microcystinu-LR (MC-LR). Cílem této studie bylo stručně shrnout dopady microcystinů (MCs) na laboratorní hlodavce (myši a krysy), kteří byli použiti v kontrolovaných podmínkách jako modelová zvířata pro vyšší savce včetně člověka.

Ve většině experimentů byl MC aplikován intraperitoneálně, protože oproti orálnímu nebo intratracheálnímu použití bylo možné lépe sledovat nepříznivý vliv na jednotlivé orgány. Lze konstatovat, že bez ohledu na způsob podávání MC hlodavcům vyvolal tento toxin vážné poškození různých orgánů, prioritně jater, kde byly zaznamenány krevní výrony a jaterní tumory, dále poškození trávicího traktu, ledvin, varlat a nadvarlat, plic, zhoršení parametrů krevní plazmy a negativní dopad na potomstvo. Kromě výše zmíněných histologických nálezů byl potvrzen dopad na biochemické ukazatele, jako jsou enzymy: GST, CAT, GR, GPX, SOD, AST, ALT, γ -GT, protein fosfatáza, SDH, a LDH nebo stresové proteiny jako HSP-70 a další parametry: GSH, celkový bilirubin, močovinový dusík, a kreatin. I když dávky MC použité během experimentů byly mnohem vyšší než ty, přirozeně se nacházející v biomase sinic a ve vodním prostředí v průběhu vegetačního období, i tak je tento cyanotoxin stále potenciální hrozbou pro savce. Jelikož jsou uvedené výsledky založené především na intraperitoneálním podávání microcystinu, ke kterému v přirozených podmínkách nedochází, při dalších experimentech by měl být kladen důraz především na orální, tracheální a transdermální aplikace.

microcystin, myši, krysy, intraperitoneální, orální, intratracheální aplikace

This work was supported by the National Agency for Agriculture Research (QH71015) and by the Research plan No. MSM6215648905 *Biological and technological aspects of sustainability of controlled ecosystems and their adaptability to climate change*, which is financed by the Ministry of Education, Youth and Sports of the Czech Republic.

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