

THE EFFECT OF SELECTED TRIAZINES ON FISH: A REVIEW

Dalibor Koutnik*, Alzbeta Stara, Josef Velisek

South Bohemian Research Center of Aquaculture and Biodiversity of Hydrocenoses, Faculty of Fisheries and Protection of Waters, University of South Bohemia in Ceske Budejovice Zatisi 728/II, 389 25 Vodnany, Czech Republic

*Corresponding author, E-mail: dkoutnik@frov.jcu.cz

Summary: Anthropogenic pollution constitutes a worldwide problem of growing concern. Increased environmental pollution can be attributed to a variety of factors associated with industrial and agricultural technologies. Triazine herbicides are among the most commonly used pesticides in the world, and are predominant class of herbicide. In recent years, concerns about the persistence, mobility and toxicity of triazines and their metabolites have been growing, owing to the detection these herbicides compounds and their of residual concentrations in different environmental compartments. The detectable levels are in drinking and ground water, food and fish, also their metabolites are frequently found in water ecosystems. Moreover, some of triazine pesticides are prohibited in European country. Eight s-triazines have been identified as relevant in a study on the prioritizing of substances dangerous to the aquatic environment in the member states of the European Community and they are included in the European Union Priority Pollutants List and the U.S. Environmental Protection Agency's List. Current knowledge about residual triazine in the aquatic environment, including status, toxic effects, and triazine in fish, are reviewed. Based on the above, we identify major gaps in the current knowledge and some directions for future research. A review contains the impact of the seven most frequently detected triazines in water (ametryne, atrazine, metribuzine, prometryne, simazine, terbuthylazine, and terbutryne) on fish physiology and acute toxicity. Toxic effect of triazine has influence mainly on growth, early development, oxidative stress biomarkers, antioxidant enzymes, hematological, biochemical plasma indices, caused histopathological changes in liver and kidney of fish.

Key words: triazine; fish; toxicity; biochemical profile; hematology; histology

Abbreviations & Units: AChE – acetylcholinesterase; ACP – acyl carrier protein; ALB – albumin; ALP – alkaline phosphatase; ALT – alanine aminotransferase; APND – aminopyrine; AST – aspartate aminotransferase; Ca – calcium; CA – carbonic anhydrase; CAT – catalase; CbE – carboxylesterase; CF – condition factor; CK – creatine kinase; CREA – creatine; CYP – cytochrome; DS – distal segments; EC – ceruloplasmin; ERND – erythromycin N-demethylase; EROD – ethoxyresorufin-O-deethylase; FRAP – ferric reducing ability of plasma; GLOB – total globulins; GLU – glucose; GSH – reduced glutathione; GPx – glutathione peroxidase; GR – glutathione reductase; Hb – hemoglobin; MRCs – mitochondria-rich cells; HSI – hepatosomatic index; Hsp – heat shock protein; iNOS – inducible nitric oxide synthase; LACT – lactate; LC50 – lethal concentration; LDH – lactate dehydrogenase; LPO – lipid peroxide; MCH – mean corpuscular hemoglobin; MCHC – mean corpuscular hemoglobin concentration; MCV – mean corpuscular volume; MDA – malondialdehyde; Mg – magnesium; Na – natrium; NCR – NADPH cytochrome P450 reductase; NH3 – ammonia; P – phosphorus; PCV – hematocrit; PD – proximal segments; PHOS – inorganic phosphate; POD – guaiacol peroxidase; PROD – pentoxyresorufin-O-deethylase; RBC – erythrocyte count; RCs – rodlet cells; ROS – reactive oxygen species; SOD – superoxide dismutase; SSI – spleen somatic index; SW – spleen weight; TAG – triacylglycerols; TBARS – thiobarbituric acid reactive substances; TP – total protein; UDPGT – UDP-glucuronosyltransferase; WBC – leukocyte count; 11-KT – 11-ketotestosterone.

Introduction

Sources of pollution constitute a problem of increasing concern all over the world (1). Increased environmental pollution can be attributed to a variety of factors resulting from different industrial and agricultural technologies (2). Agricultural development has led a parallel growth in the use of chemical agents for plague controls, which are known as pesticides. These compounds are released into the environment and due to their physico-chemical properties, such as water solubility, vapor pressure or partition coefficients between organic matter (soil or sediment) and water, they can disperse in various environmental media provoking serious health problems (3).

Effects of the residues of various substances persisting in the aquatic environment, the most important of those being pesticides, also are monitored. From among pesticides, the most frequently found are residue of triazine herbicides. Triazine herbicides are among the most commonly used pesticides in the world. The triazine was discovered in 1954 (4). The chemical structure of triazines is divided into asymmetric (metribuzine) and symmetric (atrazine, simazine, prometryne, etc.). The structures of all of the triazine herbicides have a six-member ring containing three nitrogen atoms and three carbon atoms (5). Triazines compounds are used against a wide variety of weed species. They are used primarily to selective control broad leaf and grassy weeds (6). As herbicides, the triazines may be used alone or in combination with other herbicide active ingredients to increase the weed control spectrum (7).

In recent years, concerns about the persistence, mobility and toxicity of triazines and their metabolites have been growing, owing to the detection of residual concentrations of these herbicides in groundwater and in different environmental compartments (8, 9). Moreover, some of triazine pesticides are prohibited in European countries. Triazines have been identified as relevant in a study on the prioritizing of substances dangerous to the aquatic environment in the member states of the European Community (10) and they are included in the EU Priority Pollutants List and the US Environmental Protection Agency's List. Triazine are highly toxic to moderately toxic to fish (Tab. 1.). On base of these informations, we decided to write a review about the impact of the seven most

frequently detected triazines in water (ametryne, atrazine, metribuzine, prometryne, simazine, terbuthylazine, and terbutryne) on fish.

Ametryne

Ametryne (4-N-ethyl-6-methylsulfany-2-N-propan-2-yl-1,3,5-triazine-2,4-diamine) was first registered as a pesticide use to control broadleaf weeds and annual grasses in sugarcane fields in the USA in 1964. Ametryne has also been used as a general herbicide in uncultivated areas, rights of way, and industrial areas and aquatic weeds. Over time, the uses of ametryne have been cancelled so that only four use sites remain: field corn, popcorn, pineapple, and sugarcane. Currently, only one ametryne end use product is registered. In 2005 US EPA has received requests for voluntary cancellation of all other products (37). The extensive use of ametryne in agriculture and some properties of this herbicide such as aerobic soil half-life of 53.2 days, adsorption coefficient of 3.45, and leaching potential of 6.94 (38) suggest that it could be present in the environment as a potential contaminant of soil, surface water and groundwater, and river sediment (39).

Environmental fate

Ametryne is a moderately persistent herbicide which inhibits photosynthesis and other enzymatic processes. The environmental fate of ametryne varies based on the site-specific properties of the soil to which it is applied. Based on packed soil column leaching studies, ametryne and its degradates exhibit moderate to high mobility in most sandy to loamy soils, except for clay where its mobility is low. The major route of degradation of ametryne is aerobic soil metabolism, with an observed half-life range of 9.6 days to 84 days. Ametryne is stable to hydrolysis, and degrades slowly by aquatic photolysis, half-life is 368 days (37). Major metabolite product of ametryne is deethyl ametryne (38).

Ametryne is persistent, it may leach as a result of high rainfall, floods, and furrow irrigation. Given its persistence and mobility, transport of ametryne to ground water and surface water is expected. Monitoring of ametryne concentrations in ground water and surface water is limited. In Europe rivers ametryne levels can reach values,

Table 1: Acute toxicity of triazines on fish

Exposure 96hLC50 [mg/L] (Reference)							
Species	Ametryne	Atrazine	Metribuzine	Prometryne	Simazine	Terbutylazine	Terbutryne
Guppy (<i>Poecilia reticulata</i>)	0.3 (11)	4.3 (13)	-	7.0*** (29)	-	1.6 (13)	-
Japanese eel (<i>Anguilla japonica</i>)	1.5** (12)	-	-	-	-	-	-
Rainbow trout (<i>Oncorhynchus mykiss</i>)	3.4 (13)	8.8 (13)	42.0 (24)	2.9 (14)	100.0* (14)	3.4 (14)	3.0 (13)
Sheepshead minnow (<i>Cyprinodon variegatus</i>)	5.8 (14)	13.4 (14)	85.0 (14)	5.1 (28)	4.3 (14)	-	-
Goldfish (<i>Carassius auratus</i>)	14.0 (14)	58.6 (22)	-	4.0 (14)	32.0 (14)	-	-
Fathead minnow (<i>Pimephales promelas</i>)	16.0 (14)	4.1 (15)	-	-	-	-	-
Bluegill (<i>Lepomis macrochirus</i>)	19.0 (13)	50.0 (13)	76.0 (14)	7.9 (28)	100.0 (34)	7.5 (14)	4.0 (13)
Black bullhead (<i>Ameiurus melas</i>)	25.0 (11)	35.0 (11)	-	3.0 (11)	65.0 (11)	7.0 (11)	3.0 (11)
Crucian carp (<i>Carassius carassius</i>)	27.0 (11)	100.0** (11)	-	-	100.0 (13)	66.0 (13)	4.0 (11)
Channel catfish (<i>Ictalurus punctatus</i>)	-	10.0 (16)	3.4 (23) 100.0 (24)	-	85.0 (14)	-	-
Coho salmon (<i>Oncorhynchus kisutch</i>)	-	12.0 (17)	-	-	-	-	-
Common carp (<i>Cyprinus carpio</i>)	-	18.8 (18)	175.1 (26)	8.0 (27)	40.0** (33)	-	4.0 (35)
Chinook salmon (<i>Oncorhynchus tshawytscha</i>)	-	19.0 (17)	-	-	910.0 (17)	-	-
Fera (<i>Coregonus fera</i>)	-	26.3 (19)	-	-	-	-	-
Brown trout (<i>Salmo trutta</i>)	-	27.0 (20)	-	-	70.0 (20)	-	-
Zebrafish (<i>Danio rerio</i>)	-	40.0** (21)	-	3.0 (27)	12.6 (31)	-	-
Red rasbora (<i>Rasbora heteromorpha</i>)	-	-	140.0 (25)	-	-	-	-
Red-tailed rasbora (<i>Rasbora borapetensis</i>)	-	-	145.0 (25)	-	-	-	-
Minnow (<i>Phoxinus phoxinus</i>)	-	-	-	4.5 (27)	-	-	-
Silver carp (<i>Hypophthalmichthys molitrix</i>)	-	-	-	7.0 (27)	-	-	-
Western mosquitofish (<i>Gambusia affinis</i>)	-	-	-	10.0* (30)	-	-	-
Tilapia mosambicus (<i>Oreochromis mossambicus</i>)	-	-	-	-	3.1 (31)	-	-
Barbus ticto (<i>Barbus ticto</i>)	-	-	-	-	24.5 (31)	-	-
Rohu (<i>Labeo rohita</i>)	-	-	-	-	26.9** (32)	-	-
Yellow bullhead (<i>Ameiurus natalis</i>)	-	-	-	-	110.0 (14)	-	-
genus Bullheads (<i>Ameiurus</i> sp.)	-	-	-	-	-	7.0 (13)	-
Perch (<i>Perca fluviatilis</i>)	-	-	-	-	-	-	4.0 (11)
Grass carp (<i>Ctenopharyngodon idella</i>)	-	-	-	-	-	-	8.9** (36)

* 24hLC50; ** 48hLC50; *** 72hLC50

up to 1.14 µg/L (39-41). In surface water near to Sao Paulo (Brasil) was found contamination from 0.17 to 0.23 µg/L (42, 43).

Acute toxicity

Ametryne is highly toxic to moderately toxic to fish. The lethal concentration (96hLC50) for fish is in range 0.3 to 27.0 mg/L (Tab. 1.). Ametryne is highly toxic to crustaceans and moderately to highly toxic to mollusks (44).

Effect of ametryne on fish

Although the lethal toxicity of fish to ametryne, have been well-documented, there is a dearth of data on the effects of ametryne on fish physiology. Only three studies on effects on fish physiology of ametryne have been conducted. Ametryne caused increase of plasma glucose level, hepatic glucose-6-phosphatase and decreased of muscle and liver glycogen contents in grass carp (*Ctenopharyngodon idella*) during sublethal and lethal (96hLC50) exposure (45). Acute exposure of ametryne inhibited of cholinesterase in juvenile and adult zebrafish (*Danio rerio*). Ametryne caused increase of activity glutathione S-transferase only in larvae, but not in adult fish. And they conclude that these biomarkers are a useful tool to evaluate the risk of fish exposure of ametryne, even at sublethal levels (46). Mix atrazine and ametryne in concentrations (0.5, 1.0, 1.5, and 2.0 µg/L) exposure caused micronuclei formation and erythrocytic nuclear abnormalities in zebrafish (47).

Atrazine

Atrazine (6-chloro-N2-ethyl-N4-(1-methylethyl)-1,3,5-triazine-2,4-diamine) was used for control of some annual broadleaf and grass weeds in corn, sorghum, sugar cane, orchards, vineyards and non-agricultural areas (48). Atrazine causes blockage of electron transport by Hill's reaction in plant photosynthesis (49). It is an indirect endocrine disruptor (50, 51) because it can cause convert testosterone to estrogen (52). Atrazine and plant protection products containing this substance were banned in 2005 by Commission Decision 2004/247/CE.

Environmental fate

Atrazine is toxic, persistent and bioaccumulative (53). According to its physical and chemical characteristics of the group of compounds that are moderately resistant and moderately mobile in soils. The half-life of atrazine, depending upon the environment and the amount and frequency of administration, varies between a few days to several months. The photolysis in water is very slow. An estimated half-life is 805 days. In controlled aerobic water-sediment systems atrazine was eliminated from the water with a half-life of 28-134 days, while the degradation half-life was found to be 45-253 days for the whole system (54). In European rivers atrazine levels can reach values, up to 6.47 µg/L (55), but in US rivers was about 20 µg/L (56).

Acute toxicity

Lethal acute toxicity (96hLC50) of atrazine for fish is ranging from units to hundreds milligrams per liter (Tab. 1.). Order of sensitivity to atrazine is: macrophytes > phytoplankton > zooplankton > fish > benthos (57). Fish subjected to acute exposure of atrazine herbicide displayed uncoordinated behavior. At the initial exposure, fish were alert, stopped swimming and remained static in position in response to the sudden changes in the surrounding environment. After some time they tried to avoid the toxic water with fast swimming and jumping. Faster opercula activity was observed as surfacing and gulping for air. They secreted copious amounts of mucus from whole body continuously and soon a thick layer of mucus was found deposited in the buccal cavity and gills. Body pigmentation was decreased. Ultimately fish lost their balance, consciousness, engage in rolling movement and became exhausted and lethargic. Lastly, they remained in vertical position for a few minutes with anterior side or terminal mouth up near the surface of the water, trying to gulp air and tail in a downward direction. Soon they settled at the bottom of the tank, and after some time their bellies turned upward and the fish died (58).

Table 2: The effect of atrazine on common carp

Development stage	Concentration	Exposure	Effects	Reference
Juvenile	4.28, 42.8, 428 µg/L	40 days	↑ EROD, PROD, CYP, CYP1A mRNA level in liver	(61)
Juvenile	5 mg/L	96 hours	↑ GLU; ↓ RBC, WBC	(62)
	15 mg/L		↑ GLU, TP, ALB, ALT, ALP, LDH, myelocytes ↓ WBC, lymphocytes	
	20 mg/L		↑ GLU, TP, ALT, ALP, LDH, myelocytes, ↓ P, Ca, WBC, lymphocytes	
	30 mg/L		↑ GLU, ALT, AST, LDH, myelocytes, monocytes; injection of visceral vessels, ↓ PCV, RBC, Hb, WBC, lymphocytes; dystrophic lesions of hepatocytes, teleangiectasis in gill	
Juvenile	4.28 µg/L	40 days	↑ ACP in spleen, ACP in head kidney ↓ Na ⁺ /K ⁺ -ATPase in head kidney	(63)
	42.8 µg/L		↑ ACP in spleen, ACP in head kidney, MDA in spleen, ↓ SOD in spleen, SOD in spleen, head kidney, Na ⁺ /K ⁺ -ATPase in head kidney	
	428 µg/L		↑ ACP in spleen, ACP in head kidney, MDA in spleen, head kidney ↓ ALP in spleen, ALP in head kidney, Na ⁺ /K ⁺ -ATPase in spleen, Na ⁺ /K ⁺ -ATPase in head kidney, SOD in spleen, SOD in head kidney	
Juvenile	4.28 µg/L	40 days	↑ HSP90	(64)
	4.28, 42.8, 428 µg/L	40, 80 days	↑ HSP60	
	42.8, 428 µg/L		↑ HSP70	
Juvenile	4.28, 42.8, 428 µg/L	40 days	↑ APND, ERND, mRNA levels of CYP1 family (CYP1A, CYP1B, CYP1C) in gill	(65)
Juvenile	4.28, 42.8, 428 µg/L	40 days	↑ iNOS, production of NO in brain	(66)
Juvenile	428 µg/L	40 days	↓ AChE, mRNA levels of AChE	(67)
Juvenile	42.8, 428 µg/L	40 days	↑ MDA in kidney, MDA in brain; ↓ CAT in kidney, SOD in kidney, SOD in brain, GSH-Px in kidney; GSH-Px in brain; different degrees of granule cell loss in the hippocampus, reduction of Nissl bodies, degeneration of Purkinje cells, neuropil loss; swelling of epithelial cells of renal tubules, necrosis in the tubular epithelium, contraction of the glomerulus and expansion of Bowman's space,	(68)
Juvenile	4.28 µg/L	40 days	↑ CAT in gill; CAT in liver ↓ GSH-Px in liver	(69)
	42.8, 428 µg/L		↑ MDA in liver, MDA in gill ↓ CAT in liver, CAT in gill; SOD in liver, SOD in gill, GSH-Px in liver, GSH-Px in gill; different degrees of hydropic degeneration of liver, vacuolisation, pyknotic nuclei, and fatty infiltration; varied degrees of epithelial hypertrophy in gill, telangiectasis, oedema with epithelial separation from basement membranes, general necrosis, and epithelial desquamation	
Juvenile	428 µg/L	40 days	↑ mRNA levels of IL-1 beta, mRNA levels of IL-1R1	(70)
Juvenile	4.28, 42.8, 428 µg/L	40 days	↓ RNA levels of AChE in brain and muscle	(71)
Juvenile	4.28, 42.8, 428 µg/L	40 days	↓ AChE, CbE in brain and muscle	(72)
Juvenile	< 7 µg/L	14 days	induction cytochrome P4501A1	(73)
	< 100 µg/L		↑ DNA strand breaks	
Embryo - larvae	0.3 µg/L	30 days	↑ GPx, GST, SOD, CAT, GR	(74)
	30 µg/L		↓ GR	
	100, 300 µg/L		↑ TBARS, ↓ GR	

Table 3: The effect of atrazine on zebrafish

Development stage	Concentration	Exposure	Effects	Reference
Juvenile	0.3 µg/L	28 days	↑ GPx, GR; ↓ CAT	(75)
	3 µg/L		↑ GPx; ↓ CAT	
	30 µg/L		↑ GPx, GR, SOD, TBARS; ↓ CAT	
	90 µg/L		↑ GPx, SOD, TBARS; ↓ CAT	
	25 µg/L		scattered lesions in gill	
Juvenile	90 µg/L	28 days	↓ growth rates; dystrophic lesions of hepatocytes; ↑ MRCs in filament epithelium of gill	(76)
Juvenile	2.5 µg/L	21 days	↑ SOD, CAT	(77)
	2.5, 5, 10 µg/L	14, 21 days	↑ POD	
Adult – female	10 µg/L	14 days	↑ SOD in ovary, CAT in ovary; ↓ GSH in liver	(78)
	100 µg/L		↑ SOD in liver, MDA in liver; ↓ GSH in liver	
	1000 µg/L		↑ SOD in liver, CAT in liver, MDA in liver; ↓ GSH in liver	
Adult – female	0.01, 0.1, 1 mg/L	10, 15 days	↑ cytochrome P450 content, APND, ERND	(79)
	0.01, 0.1, 1 mg/L	20, 25 days	↑ APND, ERND, NCR	
Adult – male	0.01, 0.1, 1 mg/L	10, 15 days	↑ cytochrome P450 content, NCR, APND, ERND	
	0.1 mg/L	20, 25 days	↑ cytochrome P450 content, APND	
Embryo - larvae	4 mg/L	48 hours	disturbed the normal development to long pec stage	(80)
	10-20 mg/L		retardations in organogenesis, a slowdown of movements, and functional disturbances of heart and circulatory system	
Embryo - larvae	5 mg/L	48 hours	↑ soluble (s) and microsomal (m) GST	(81)

Effect of atrazine on fish

Effects of atrazine on fish physiology, have been well-documented. Its effect is the best described from all triazines. Atrazine affected hematological, biochemical profile, antioxidant enzymes, oxidative stress indices, growth and caused histopathological changes in tissues. The effects of atrazine are mentioned on carp (Tab. 2.), zebrafish (Tab. 3.), Salmonidae (Tab. 4.), other fish (Tab. 5.). In a study conducted by Ventura et al. (59), it was observed that the herbicide atrazine has a genotoxic and mutagenic effect. In this study, the authors observed that the herbicide can interfere in the genetic material of the organisms

exposed, even at doses considered residual, which led the authors to suggest that residual doses of atrazine, resulting from leaching of soils of crops near water bodies, can interfere in a negative form in the stability of aquatic ecosystems. The bioaccumulation factors for atrazine in the liver, muscle, heart, gonads and brain of banded tilapia (*Tilapia sparrmanii*) is ranged from 0.9 to 20.0 (60).

Metribuzine

Metribuzine (4-amino-6-tert-butyl-3-(methylthio)-1,2,4-triazin-5-one) is an asymmetrical triazine herbicide. It is distinct from the symmetrical

Table 4: The effect of atrazine on Salmonidae

Species	Concentration	Exposure	Effects	Reference
Rainbow trout (<i>Oncorhynchus mykiss</i>) Juvenile	555 µg/L	4 days	↑ cortisol, monocytes; ↓ SSI, lymphocytes	(82)
Atlantic salmon (<i>Salmo salar</i> L) Smolts	100 µg/L	21 days	↓ feeding, Cl ⁻ , Mg ²⁺ , Na ⁺ , Ca ²⁺ ; ↑ cortisol	(83)
Atlantic salmon (<i>Salmo salar</i> L) Smolts	2 µg/L	7 days	↓ Na ⁺ K ⁺ ATPase in gill	(84)
	5, 10 µg/L		↑ cortisol; ↓ Na ⁺ K ⁺ ATPase in gill	
Atlantic salmon (<i>Salmo salar</i> L) Smolts	atrazine (1 µg/L) + 4-nonylphenol (5 µg/L)	7 days	↑ Na ⁺ K ⁺ ATPase in gill, plasma Cl ⁻ , Na ⁺	(85)
	atrazine (2 µg/L) + 4-nonylphenol (10 µg/L)		↑ plasma Cl ⁻ , Na ⁺ ; ↓ Na ⁺ K ⁺ ATPase in gill	
Atlantic salmon (<i>Salmo salar</i> L.) Adult - male	above 0.04 µg/L	shorten	↓ 17,20 beta-dihydroxy-4-pregnen-3-one in plasma and milt	(86)
Rainbow trout (<i>Oncorhynchus mykiss</i>) Renal tubules	10, 20, 40, 80, 160 µg/L	4 weeks	In PS I - proliferation of smooth endoplasmic reticulum, atypical mitochondria and lysosomes, as well as gradual alterations of the apical plasmalemma; In PS II - cells proliferation of peroxisomes, ring- and cup-shaped mitochondria, alterations in the basal labyrinth; in DS cells, proliferation of atypical mitochondria with longitudinally oriented cristae, disorganization of Golgi fields and vacuolization of the cell base.	(87)

triazines such as atrazine and simazine, in which the central ring structure has alternating carbon and nitrogen atoms, in that metribuzin possesses two nitrogen atoms and two adjacent carbon atoms. It was first registered as a pesticide in the U.S. in 1973. Metribuzine is used to selectively control certain broadleaf weeds and grassy weed species on a wide range of sites including vegetable and field crops, turf grasses in recreational areas, and non-crop areas (103). Metribuzine is applied by various methods including aerial, chemigation, and ground application (103, 104).

Environmental fate

Metribuzine, like other triazine and triazinone herbicides, is prone to runoff into surface waters due to its physical and chemical characteristics: water solubility 1.220 mg/L; K_{oc} 41; vapor pressure 1.3 mPa; and soil half-life 30 days (104, 105). The degradation of metribuzine is through photochemical, chemical and biochemical deamination. Aqueous photolysis of metribuzin is rapid with a half-life of <1 day, and this clearly

contributes to the half-life of <7 days in natural pond water. Contamination of waters could result from spray and vapour drift, runoff or leaching from treated land, or from accidental spills. Measured environmental concentrations of metribuzine in water are usually low, with maximum concentrations below 1.8 µg/L (106), but modelling studies have indicated that metribuzine can reach concentrations as high as 390 g/L in surface water runoff (104).

Acute toxicity

During the acute exposure of metribuzine fish show increased respiration and loss of movement and coordination. Fish lying on the bottom of the tank and moving in circles, followed by a short excitation stage (convulsions). Necropsy after acute exposure can reveal increased watery mucus on body surfaces, black pigmentation of the skin, and abdominal distention with generalized edema. The body cavity contains transudate, and hyperemia of visceral organs and ascites (26).

Acute toxicity 96hLC₅₀ of metribuzine for fish

Table 5: The effect of atrazine on other fish

Species	Concentration	Exposure	Effects	Reference
<i>Rhamdia quelen</i> Juvenile	2, 10, 100 µg/L	96 hours	↓ CAT, GST, GPx, GR, leukocyte infiltration, hepatocyte vacuolization like steatosis and necrosis areas, leading to raised lesion index levels in all tested concentrations. ↑ free melanomacrophage	(88)
<i>Prochilodus lineatus</i> Juvenile	2, 10 pg/L	24, 48 hours	↓ EROD, ROS, CAT, SOD, GPx, GR, MDA in liver	(89)
Silver catfish (<i>Rhamdia quelen</i>) Juvenile	1.02 mg/L	24 hours	↓ bactericidal activity of the serum, bacteria agglutination, total serum peroxidase activity	(90)
<i>Prochilodus lineatus</i> Juvenile	10 µg/L	14 days	↑ GST, SOD, CAT, LPO	(91)
	25 µg/L		scattered lesions in gill	
<i>Prochilodus lineatus</i> Juvenile	25 µg/L	48 hours	↓ osmolarity	(92)
		14 days	↓ CA; ↑ Na ⁺ , Cl ⁻ , MRCs in filament epithelium of gill	
<i>Rhamdia quelen</i> Juvenile	0.73 mg/L	96 hours	↓ intracelomatic cells, phagocytic index	(93)
Fathead minnow (<i>Pimephales promelas</i>) Adult	0.5, 5.0, 50 µg/L	30 days	↓ production of egg; pathological lesions in testes: granulomatous inflammations, mineralized material in testicular tubules and efferent ducts at rates, variably-sized perinucleolar stage oocytes	(94)
Green Snakehead (<i>Channa punctata</i>) Juvenile	4.238 mg/L	5, 7, 10, 15 days	↑ SOD	(58)
	5.3, 10.6 mg/L		↑ SOD, TBARS, CAT	
Rare minnow (<i>Grobioocypris rarus</i>) Adult – male	333 µg/L	28 days	↑ HSI, hypertrophy of hepatocytes	(95)
Rare minnow (<i>Grobioocypris rarus</i>) Adult	3, 10 µg/L	28 days	lesions in gill including hyperplasia, necrosis in epithelium region, aneurysm and lamellar fusion lesions in kidney included extensive expansion in the lumen, degenerative and necrotic changes of the tubular epithelia, shrinkage of the glomerulus, increase of the Bowman's space	(96)
<i>Caquetaia kraussii</i> Juvenile	2.5 µg/L	72 hours	hepatocytes lost the cytoarchitecture (the hepatocytes have different diameters and irregular contour); isolated associations between mitochondria and rough endoplasmic reticulum in the cytoplasm	(97)
<i>Rhamdia quelen</i> Juvenile	3.5, 5.25 mg/L Herbimix® (simazine + atrazine)	96 hours	↑ cortisol	(98)
Goldfish (<i>Carassius auratus</i> L.) Juvenile	1 000 µg/L	56 days	↑ 11-KT	(99)
Red drum (<i>Sciaenops ocellatus</i>) Larvae	40, 80 µg/L	4 days	↓ growth; behaviour: swam significantly faster, with a higher rate of travel, active swimming speed, hyperactive, swam considerably more convoluted paths compared to control	(100)
Goldfish (<i>Carassius auratus</i>) Juvenile	0.5 µg/L	24 hours	↓ sheltering, grouping behavior, burst swimming; ↑ surfacing activity	(101)
Mormyrid fish (<i>Gnathonemus petersii</i>) Juvenile	0.5, 5 mg/L	6 hours	breaks in the gill epithelium, which developed into deep pits	(102)

is ranging from units to hundreds milligrams per liter (Tab. 1.).

Effect of metribuzine on fish

The effects of metribuzine on fish physiology have been well-documented. Metribuzine affected hematological, biochemical profile, growth and caused hitopatological changes in tissues (Tab. 6.). During acute poisoning of metribuzin in rainbow trout (*Oncorhynchus mykiss*) or common carp (*Cyprinus carpio*), the following clinical symptoms are observed: accelerated respiration, loss of movement coordination, fish lying on their flanks and moving in this position. The subsequent short excitation stage (convulsions, jumps above the water surface, movement in circles) changes into a resting stage and another short-time excitation follows again. In the end, fish fall into damp, moving mainly on their flanks. The respiration is slowed down, and the damp phase and subsequent agony are very long. Fish are produced of watery mucus on body surfaces, the skin is matt dark in colour and the ventricle expansion. The body cavity contained transudate, and an increased injection of visceral vessels is also obtained (26, 107).

Prometryne

Prometryne (2,4-bis(isopropylamino)-6-methylthio-s-triazine) was the first effective herbicide for several crops, making it a true pioneer herbicide in the methylthiotriazine class of chemistry (112) and was first registered in 1964 by Ciba Crop Protection (113). Prometryne is selective herbicide of the s-triazine chemical family, has been utilized as a pre- or post-emergence controller of annual grasses and broadleaf weeds in a variety of crops, including cotton, celery, pigeon peas and dill. Prometryn's mechanism of action inhibits the electron transport in susceptible species (114). Prometryne application is not permitted in Europe, but is widely used in China (115), Australia, Canada, New Zealand, South Africa, and the United States (28).

Environmental fate

Prometryne is usually soil-applied and relatively water soluble, it tends to accumulate in

crops (114). Prometryne binds readily to soils with high clay and organic matter content. Available data indicate that this herbicide is mobile in sandy soils and moderately mobile in sandy loam soils. Its mobility appears to be related to organic content of the soil. Prometryne the lower the organic content, the more mobile prometryne is in soil. Prometryne is adsorbed to a greater extent than most other commercial triazine herbicides (116). Prometryn is a persistent chemical, it is persists in the soil from one to three months. Its soil half-life is 60 days. Following multiple annual applications of the herbicide, prometryne activity can persist for 12-18 months after the last application. It will persist longer under dry or cold conditions which are not conducive to chemical or biological activity. It resists abiotic hydrolysis, direct photolysis, and biodegradation under anaerobic conditions. Its half-life under aerobic conditions is in excess of 270 days (117).

Significant traces of prometryne are documented in the environment, mainly in water, soil, and plants used for human and domestic animal consumption. Maximal environmental concentration prometryne is 0.51 µg/L in the Czech rivers (14). In surface waters of Greece, prometryne has been recorded at concentrations from 0.19 to 4.40 µg/L (118). Prometryne to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece, during 1992–1994 were detected at concentrations occasionally exceeding 1 µg/L (118). In surface water of Western France, remains of prometryne were detected at concentrations from 0.1 to 0.44 µg/L (119).

Acute toxicity

Exposure prometryne to nontarget organisms can result from direct applications, spray drift, and runoff from treated areas. Studies indicate that prometryne poses an acute risk to nonendangered and endangered terrestrial and aquatic plants (113). Prometryne is toxic to fish (Tab. 1.). The most sensitive aquatic organisms are freshwater algae (14).

Effect of prometryne on fish

Although the lethal toxicity of fish to prometryne, have been well-documented, there is a dearth of data on the effects of prometryne on fish physiology.

Table 6: Effect of metribuzine on fish

Species	Concentration	Exposition	Effects on fish	Reference
Bluegill (<i>Lepomis macrochirus</i>) Juvenile	9, 19, 38, 75 µg/L	6 weeks	No effects on fish survival and growth	(103)
Rainbow trout (<i>Oncorhynchus mykiss</i>) Juvenile	89.3 mg/l Sencor 70 WG (active substance 70% of metribuzin)	96 hours	↓ TP, TAG, AST, NH ₃ , Ca, LACT, ALP, RBC, PCV, lymphocyte coun. ↑ MCH, relative and absolute count of neutrophile granulocytes Revealed mild proliferation of goblet cells of the respiratory epithelium of secondary gill lamellae and hyaline degeneration of epithelial cells of the renal tubules of the caudal kidney.	(107)
Common carp (<i>Cyprinus carpio</i>) Juvenile	1.75 mg/L	28 days	↑ RBC, PCV	(108)
Common carp (<i>Cyprinus carpio</i>) Juvenile	250.2 mg/L Sencor 70 WG (active substance 70% of metribuzin)	96 hours	↑ GLU, NH ₃ , Ca, monocytes, neutrophile granulocytes, developmental forms myeloid sequence, basophiles. ↓ TP, ALB, GLOB, TAG, LDH, LACT, PHOS, PCV, Hb, MCV, WBC, lymphocyte Revealed hyaline degeneration of the epithelial cells of renal tubules of the caudal kidney.	(26)
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	0.9, 4, 14, 32 mg/L	30 days	↑ GST	(109)
	0.9, 4, 14 mg/L		↑ GR	
	0.9 mg/L		↑ TBARS	
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	0.9, 4, 14, 32 mg/L	30 days	↓ specific growth rate, body weight, length	(110)
	32 mg/L		Diffuse vacuolization of the cytoplasm of hepatocytes, often with compression of nuclei at the periphery of the cells. Monocellular necroses of hepatocytes. Eosinophilia of tubular epithelial cells with coagulation of cytoplasm and desquamation of necrotic cells into the lumen of proximal tubules in the caudal kidney.	
Zebrafish (<i>Danio rerio</i>) Juvenile	33, 55 mg/L	28 days	↓ specific growth rate, body weight, length	(111)
	55 mg/L		Moderate dystrophic lesions of hepatocytes, initial cell injury represented by diffuse hydropic to vacuolar degeneration of hepatocytes.	

Only three studies on effects of prometryne on carp physiology have been conducted (Tab. 7.). Chronic exposure has no influence on growth, oxidative stress biomarkers and it has influence on hematological, biochemical plasma indices, antioxidant enzymes and caudal kidney (120-122).

Simazine

Simazine (6-chlor-N₂,N₄-diethyl-1,3,5-triazin-2,4-diamin) is one of the first compound triazines (a six-membered ring containing three carbon and three nitrogen atoms), was introduced by a Swiss company J. R. Geigy in 1956 and was registered

in 1957 (5). From 1990 to 1993 are among the most widely used herbicides in the U.S. Simazine belongs to a group of selective triazine herbicides, is used for a pre- and post-emergence control most weeds field crops as well as in non-crop areas. When applied to the soil is absorbed by leaves and roots, causing inhibition of photosynthesis in whole plants (123). It is biodegradable, is metabolized in plants and soil, both chemical, and microbiological processes (112). It is fairly resistant to physical and chemical dissipation processes in the soil. It is persistent and mobile in the environment (124). Even before 1992 simazine was used to kill submerged (growing in water) weeds and algae in large aquariums, ponds, swimming

Table 7: Effect of prometryne on fish

Species	Concentration	Exposition	Effects on fish	Reference
Common carp (Cyprinus carpio) Embryo - larvae	0.51, 80, 1 200 µg/L	35 days	↓ GR activity	(120)
Common carp (Cyprinus carpio) Juvenile	80 µg/L	14 days	↓ GR in brain, SOD in intestine	(121)
	8, 80 µg/L		↓ SOD in gill, ↑ SOD in brain	
	0.51, 8, 80 µg/L		↑ GR in muscle	
	8, 80 µg/L	30 day	↓ SOD in brain	
	0.51, 8, 80 µg/L		↓ SOD in gill	
	80 µg/L	60 days	↑ CAT in intestine, ↓ CAT liver, SOD in gill	
Common carp (Cyprinus carpio) Juvenile	80 µg/L	30 days	↑ GLU	(122)
	8, 80 µg/L	60 days	↑ GLU, MCH, MCHC, Hb ↓ SW, LACT	
	0.51, 8, 80 µg/L	30, 60 days	↑ CK, ALT, ↓ AST, Ca, Mg, PHOS	
		60 days	Hyaline degeneration of the epithelial cells of caudal kidney tubules	

pools or cooling towers (125). Simazine and plant protection products containing this substance were banned in 2004 by Commission Decision 2004/247/CE. The presence of simazine in the soil-water system is considered an environmental hazard, and, because of its estrogenic effect on various cell lines in laboratory experiments, it has recently become subject to control (6, 126).

Environmental fate

Simazine in soil and groundwater is moderately persistent with an average field half-life of 60 days. Soil half-lives have been reported of 28-149 days (127). Residual activity may remain for a year after application (2 to 4 kg/ha) in high pH soils. Simazine is moderately to poorly bound to soils (105). Simazine is metabolized in plants and soil, both chemical, and microbiological processes (125). It does, however, adsorb to clays and mucks. Its low water solubility, however, makes it less mobile, limiting its leaching potential. Simazine has little, if any, lateral movement in soil, but can be washed along with soil particles in runoff. Simazine is subject to decomposition by ultraviolet radiation, but this effect is small under

normal field conditions. Loss from volatilization is also insignificant. In soils, microbial activity probably accounts for decomposition of a significant amount of simazine in high pH soils. In lower pH soils, hydrolysis will occur (48).

Simazine can be persistent in aquatic systems, particularly in shallow, well-mixed lakes and ponds (128). Residues may persist up to 3 years in soil under aquatic field conditions. Dissipation of simazine in pond and lake water has been found to be variable, with half-life ranging from 50 to 700 days (105). Slow biodegradation of simazine may occur in water, similar to that observed in soil. Simazine may undergo hydrolysis at lower pH. It does not readily undergo hydrolysis in water at pH = 7 (48). Simazine and its degradation products are detected less frequently than atrazine in the aquatic environment.

Simazine is the second most commonly detected pesticide in surface and ground waters in the U.S., Europe, and Australia. Simazine, and its major degradation products (deisopropyl atrazine and diamino chlorotriazine), have been extensively monitored in 20 counties in California with concentrations ranging from 0.02 to 49.2 µg/L (129, 130). Simazine levels can reach values, up to 5.0 µg/L in European rivers (131-134).

Table 8: Effect of simazine on fish

Species	Concentration	Exposition	Effects on fish	Reference
Seabream (<i>Sparus aurata</i>) Larvae	4.5 mg/L	72 hours	Cellular alterations related to loss of cellular shape in hepatocytes, lipid inclusions, focal necrosis and abundant nuclear pyknosis in the hepatocytes.	(136)
Common carp (<i>Cyprinus carpio</i>) Juvenile	45 µg/L	90 days	↑ mucus production during the experiment, Hyperplasia of epithelial cells of secundary lamellae, slight necrosis	(137)
Goldfish (<i>Carassius auratus</i>) Adult	50 µg/L Σ atrazine + simazine + diuron + isoproturon	4, 8, 12 weeks	↑ plasma lysozyme activity; production of O ₂ – in spleen, kidney; SOD in spleen and liver; ↓ antibody titre, CAT in liver, spleen, kidney	(138)
Common carp (<i>Cyprinus carpio</i>) Juvenile	45 µg/L	90 days	↓ AChE in brain and muscle	(139)
Rhamdia quelen Juvenile	16.6%, 33% 50% 96h LC50 hatrazine + simazine (Herbimix™)	96 hours	Decreased capacity in exhibiting an adequate response to cope with stress and in maintaining the homeostasis, with cortisol level lower than that in the control fish	(140)
Common carp (<i>Cyprinus carpio</i>) Juvenile	4, 20, 50 µg/L	28 days	↑ PCV, lymphocytes, developmental phases –myeloid sequence, GLU, LDH, CK, CREA; ↓ MCHC, neutrophil granulocytes bands, NH ₃ , AST Decline in hematopoietic tissue in caudal kidney; steatosis, hyperaemia, and necrosis in liver	(141)
Common carp (<i>Cyprinus carpio</i>) Juvenile	45 µg/L	15, 30, 45, 90 days	No effect on muscle LACT, LDH	(142)
			↑ mucus hyperproduction in gills and skin; No effect on MDA and GSH	(143)
		90 days	↑ PCV, necrotic areas in hematopoietic and excretory tissues of the kidneys; Isolated necrotic areas in liver	(144)
Rhamdia quelen Juvenile	16.6% 96h LC50 hatrazine + simazine (Herbimix™)	96 hours	↑ plasma cortisol	(145)
Zebrafish (<i>Danio rerio</i>) Juvenile	60 µg/L	28 days	Hypertrophy, hyperplasia of epithelial gill cells with lamellar fusion. Initial cell injury represented by swelling and hydroscopic vacuolar degeneration of hepatocytes). Coagulation of the apical part of the cytoplasm of epithelial cells of the renal tubules	(146)
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	60 µg/L	35 days	Alteration of tubular system included destruction of tubular epithelium with or without casts, vacuolization of tubular epithelia and disintegration of glomerules	(147)
	0,6, 3 mg/L		↓ growth; alteration of tubular system included destruction of tubular epithelium with or without casts, vacuolization of tubular epithelia and disintegration of glomerules	
Common carp (<i>Cyprinus carpio</i>) Juvenile	0.06 µg/L	90 days	↑ ALP; ↓ WBC; hyaline degeneration of the epithelial cells of renal tubules of the caudal kidney	(148)
	1, 2 µg/L		↑ HSI, ALP, AST; ↓ WBC; hyaline degeneration of the epithelial cells of renal tubules of the caudal kidney	
	4 µg/L		↑ HSI, TP, ALB, AST, ALP; ↓ WBC hyaline degeneration of the epithelial cells of renal tubules of the caudal kidney	

Common carp (Cyprinus carpio) Juvenile	0.06 µg/L	28 days	↑ GSH in liver;	(149)
		60 days	↑ CAT in muscle, GSH in liver	
	2 mg/L	14 days	↑ SOD in muscle; CAT in muscle, liver; GSH in liver; ↓ GPx in liver	
		28 days	↑ SOD in muscle CAT in muscle, liver; GSH in liver; ↓ GPx in liver	
		60 days	↑ ROS in liver; GSH in liver, brain; ↓ SOD in muscle; CAT in muscle, liver;	
	4 mg/L	14 days	↑ CAT in liver; SOD in muscle; GSH in liver, brain; ↓ GPx in liver	
		28 days	↑ ROS in liver; SOD in muscle; GSH in liver, brain; ↓ GPx in liver	
		60 days	↑ ROS in muscle, brain, liver; GST in brain; ↓ GST and GPx in liver, SOD in muscle; CAT in brain, liver, muscle	

Acute toxicity

Simazine was identified as relevant a study of the prioritization of substances dangerous to the aquatic environment in the member states of the European Community (10). Lethal acute toxicity for fish is ranging from units to hundreds milligrams per liter (Tab. 1.).

Effect of simazine on fish

The effects of simazine mainly on carp physiology have been well-documented in laboratory studies. Chronic exposure of simazine has influence mainly on growth, oxidative stress biomarkers, antioxidant enzymes, hematological, biochemical plasma indices, and caused histopathological changes in gill, liver and kidney (Tab. 8.). Simazine has been recently reported as suspected endocrine disruptors, it is also known to cause multiple types of cancers (135).

Terbuthylazine

Terbuthylazine (N-tert-butyl-6-chloro-N'-ethyl-1,3,5-triazine-2,4-diamine) was registered in the United States in 1975 (150). Terbuthylazine is herbicide that belongs to the chlorotriazine family, is used in both pre- and post-emergence treatment of a variety of agricultural crops and in forestry (118). Terbuthylazine have very similar chemical structure to atrazine. The difference is only iso-butyl and tert-butyl substituent on the amino

group. The minimum difference in structure affects the decomposition reactions of these substances in the environment that led to a ban on atrazine in the European Union. The EU had more stringent drinking water standards caused farmers to shift from atrazine to terbuthylazine. Terbuthylazine is used as a substitute for atrazine since the end of 2006 (151). Terbuthylazine breaks down much more rapidly than atrazine in both soil and water, and is therefore believed less likely to contaminate drinking water (152).

Environmental fate

Terbuthylazine is stable to hydrolysis, and to aqueous photolysis. It degrades very slowly under aerobic aquatic conditions, and will persist under most aquatic conditions (150). Terbuthylazine is a slightly basic, slightly water soluble triazine herbicide or algicide which adsorbs to soil organic matter. Degradation of terbuthylazine in natural water depends on the presence of sediments and biological activity (124). Under laboratory conditions, aquatic photolytic half-lives ranged from around 3 hours (attenuated) to a more realistic 1.5-5 days under more usual test conditions that seem to be reflected in the recommended use pattern. Usually, the main degradation product was hydroxy-terbuthylazine, although with an attenuator N-dealkylation is favoured. Laboratory studies in soils (sandy loam) gave half-lives of 73-138 days at 20-25 °C, but this extended to 456 days at 10 °C, with hydroxy-terbuthylazine and desethyl-terbuthylazine as the

Table 9: Effect of terbuthylazine on fish

Species	Concentration	Exposition	Effects on fish	Reference
Rainbow trout (<i>Oncorhynchus mykiss</i>) Juvenile	35.1, 42.9, 45.8 µg/L	7 days	↓ EROD, UDPGT	(159)
European sea bass (<i>Dicentrarchus labrax</i> L.) Juvenile	3.55, 5.01, 7.08 mg/L	24 hours	↑ RCs in gills, intestine, kidney histopathological examination displayed cellular and/or ultrastructural alterations in all the organs examined. In the gills necrosis, lamellar and cellular oedema, epithelial lifting, telangectasia, and fusion of secondary lamellae were encountered. The liver presented myelin-like figures, cytoplasmic rarefaction and acute cell swelling of hepatocytes. The renal tubular epithelial cells, exhibited 'blebs'.	(158)
		48 hours	↑ RCs in gills, intestine histopathological examination displayed cellular and/or ultrastructural alterations in all the organs examined. In the gills necrosis, lamellar and cellular oedema, epithelial lifting, telangectasia, and fusion of secondary lamellae were encountered. The liver presented myelin-like figures, cytoplasmic rarefaction and acute cell swelling of hepatocytes. The renal tubular epithelial cells, exhibited 'blebs'.	
Common carp (<i>Cyprinus carpio</i>) Juvenile	550 µg/L	91 days	↑ TAG, ALB, Na, TP, EC, FRAP ↓. MCHC, MCH, MCV, AST, P	(160)
	60 µg/L		↑ TAG, ALB ↓. MCH, MCV, AST, P	
	380 ng/L		↑ HSI, CF, TAG, TP	
Common carp (<i>Cyprinus carpio</i>) Juvenile	13.0 mg/L Gardoprim Plus Gold 500 SC (corresponding to 2.25 mg/L terbuthylazine and 3.75 mg/L S-metolachlor	96 hours	↑ GLU, AST, NH ₃ , LDH ↓ lymphocyte counts, WBC, PCV, PHOS, TAG, chlorides lesions in gills and liver	(161)
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	520 µg.L ⁻¹	30 days	↑ GR	(109)
Zebrafish (<i>Danio rerio</i>) Juvenile	400 µg/L	28 days	↑ GST	(162)
	700 µg/L		↑ GR, GST, pathological changes in the liver	
	1000 µg/L		↑ GR, GST, TBARS, pathological changes in the liver	
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	520, 820 µg/L	30 days	↓ specific growth and body weight, delay in development, mild leisons in liver including diffuse formation of smal round to oval vacuoles in the cytoplasma of hepatocates	(163)
Common carp (<i>Cyprinus carpio</i>) Juvenile	3.3 mg/L	24 hours	↑ GLU, AST, ALT, natrium, chlorides, phosporus, Ca, circulation disorders in gills represented by abundant presence of capillary aneurysms in gill filaments and a local hyperplasia of respiratōry epithelium	(164)
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	0.0029, 0.07, 1.4, 3.5 mg/L terbuthylazine-2-hydroxy	26, 35 days	↓ SOD, specific growth and body weight	(165)
	1.4, 3.5mg/L terbuthylazine-2-hydroxy	35 days	damage to caudal kidney tubules, delay in development	

Table 10: Effect of terbutryne on fish

Species	Concentration	Exposition	Effects on fish	Reference
Rainbow trout (<i>Oncorhynchus mykiss</i>) Juvenile	28.3 29.2, 32.6 µg/L	7 days	↓ EROD, UDPGT	(159)
Seabream (<i>Sparus aurata</i>) Larvae	2.5 mg/L terbutryn+triasulfuron	72 hours	cellular alterations related to loss of cellular shape of hepatocytes and intense nuclear pyknosis in the hepatocytes	(175)
Zebrafish (<i>Danio rerio</i>) Juvenile	0.6 mg/L	28 days	↓ specific growth; weight, damage to tubular system of kidneys	(176)
Common carp (<i>Cyprinus carpio</i>) Juvenile	2, 20, and 40 µg/L	28 days	↑ RBC, NH ₃ , AST, LDH, CK, LACT ↓ MCV, MCH, CK Diffused steatosis of the liver - the loss of cellular shape and the presence of lipid inclusions in hepatic cells; damage to caudal kidney tubules	(177)
Common carp (<i>Cyprinus carpio</i>) Juvenile	0.2, 2 µg/L	90 days	↑ RBC, MCHC, neutrophil granulocyte bands, GLU, AST, LDH, LACT, TBARS in brain, liver; CP in brain, gill; SOD in liver, brain ↓ WBC, MCV, CK, Mg, GR in liver, intestine	(178)
	0.02 µg/L		↑ TBARS in brain, liver, SOD in liver ↓ GR in liver	
Common carp (<i>Cyprinus carpio</i>) Embryo - larvae	2 mg/L	30, 36 days	↓ CF	(179)
	0.2, 2 mg/L		delay in development	
	0.02, 0.2, 2 mg/L		Alteration of tubular system in caudal kidney included destruction of tubular epithelium with or without casts, vacuolization of tubular epithelia and disintegration of glomeruli	
	0.00002, 0.02, 0.2, 2 mg/L		↓ mass and total length; damage to caudal kidney tubules	

main degradation products (153). Terbutylazine photo-degrades in water this is likely to be the main degradation pathway. The fate of residues in aerobic and anaerobic aquatic conditions is similar. The major metabolites of terbutylazine are the de-chlorinated and N-dealkylated products, which are more mobile than the parent, and exhibit some herbicidal activity when they retain the chlorine atom on the triazine ring plus one alkyl group (152, 153).

Terbutylazine levels can reach values up to 2.9 µg/L in Europe rivers (40, 154, 155). The groundwater situation in different countries was surveyed by the French Ministry of Agriculture and Fisheries. In Germany and Sweden 22 out of 3204 samples and 6 out of 230 samples were positive for terbutylazine (above 0.1 µg/L), respectively (156).

Acute toxicity

The ecotoxicity profile of terbutylazine is typical for a herbicide, with toxic effects mostly apparent towards plants/algae. However, terbutylazine shows slight toxicity towards fish and shellfish, and variable toxicity towards aquatic crustaceans, from very highly toxic to practically non-toxic (124). Standard toxicity tests with various fish species as nontarget organisms revealed LC₅₀ values between 4.6 and 66 µg/L (Tab. 1.). As a consequence, terbutylazine might be considered as a moderately or slightly toxic. The acute exposure to terbutylazine, however, leads to significant alterations of the average swimming velocity on the fish. After a nonuniform initial phase of swimming irritation, an increase in motility can be observed. With every exposure tested, this hyperactivity exceeded any preexposure motility (157).

Effect of terbutylazine on fish

Exposure to terbutylazine affected on growth, oxidative stress biomarkers, hematological, biochemical plasma indices, antioxidant enzymes, detoxification enzymes and caused the histopathological changes in gill, liver, intestine and kidney (Tab. 9.). Fish during the terbutylazine intoxication showed uncoordinated swimming and hyporeflexia increasing (158).

Terbutryne

Terbutryne (N2-tert-butyl-N4-ethyl-6-methylthio-1,3,5-triazine-2,4-diamine) was used as a selective pre- and early post- emergence controll agent of most grasses and many annual broadleaved weeds for a variety of crops, such as cereals, legumes, and tree fruits. It is also used as a herbicide for control of submerged and free-floating weeds and algae in water courses, reservoirs, and fish ponds (166, 167). Large quantities of terbutryne have been used since the mid-1980s (168). Terbutryne and plant protection products containing this substance were banned in 2005 by Commission Decision 2004/247/CE.

Environmental fate

Terbutryne degrades slowly, with a half-life of 240 and 180 days in pond and river sediments, respectively (169). Its tendency to move from treated soils into water compartments through water runoff and leaching has been demonstrated, and residual amounts of terbutryne and its metabolites have been found in drinking water and industrial food products long after application (170). The application of terbutryne has been banned in many countries because it has the potential to bioaccumulate in organisms, but it has been still detected in water environment (171). The highest concentration reported in surface water in the Weschnitz River, Germany, at a maximal concentration of 5.6 µg/L from September 2003 to September 2006 (172). Terbutryn was also detected in Mediterranean coastal waters at a concentration of 5-184 ng/L (173).

Acute toxicity

Acute toxicity 96hLC50 of terbutryne for fish is ranging from units of milligrams per liter. Terbutryne is toxic to fish (Tab. 1.).

Effect of terbutryne on fish

The effects of terbutryne mainly on carp, zebrafish and rainbow trout, physiology have been documented in laboratory studies. Chronic exposure of terbutryne has influence mainly on growth, oxidative stress biomarkers, antioxidant enzymes, hematological, biochemical plasma indices, caused histopathological changes in liver and kidney (Tab. 10.). The results demonstrate that the terbutryne accumulated to a somewhat greater extent in the viscera (liver, intestine, and pyloric caeca) than in the muscle tissue of the carp and trout during exposure (169, 174). Bioconcentration factors (BCFs) of terbutryne for fish were estimated 312 (169).

Conclusion

Triazines are predominant class of herbicide. They are most frequently detected pesticide in aquatic environment. Moreover, some of triazine pesticides are prohibited in European countries. Triazines have been identified as relevant in a study on the prioritizing of substances dangerous to the aquatic environment in the member states of the European Community and they are included in the EU Priority Pollutants List and the US Environmental Protection Agency's List. All of above cited seven triazines are banned or severely restricted in EU (180). Acute toxicity was assessment on 28 fish species. Toxic effect of triazine has influence mainly on growth, early development, oxidative stress biomarkers, antioxidant enzymes, hematological, biochemical plasma indices, caused histopathological changes in liver and kidney. Investigation of triazine and their metabolites properties in connection with environment, chronic effects and potential bioaccumulation must continue thoroughly. Research on non-target species should be really detailed and should continue because as can be seen in the previous text, triazines are able to cause pathological changes in fish. We assume

that triazines and their metabolites have similar effects on other non-target organisms as to have on fish. As shown some studies on crayfish (181–183). It is necessary to focus on the research of triazines metabolites using new molecular techniques and gene expression.

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UČINEK TRIAZINSKIH HERBICIDOV NA RIBE: PREGLED

D. Koutnik, A. Stara, J. Velisek

Povzetek: Onesnaževanje okolja je svetovni problem, ki povzroča vse večjo zaskrbljenost in je posledica različnih človekovih dejavnosti povezanih z industrijo in kmetijstvom. Triazinski herbicidi so med najpogostejše uporabljenimi pesticidi. V zadnjem času vse bolj naraščata zavedanje in zaskrbljenost zaradi njihove široke uporabe, saj so ostanki in presnovki triazinov zelo obstojni in se kopičijo v različnih delih okolja. Triazini so bili zaznani tudi v vodnih ekosistemih, v pitni vodi in podzemnih vodah ter tudi v ribah. Zato je uporaba določenih triazinskih pesticidov v evropskih državah že prepovedana. Osem s-triazinov je bilo uvrščeno v študijo za pripravo prednostnega seznama snovi, nevarnih za vodno okolje v državah članicah Evropske unije in so že vključeni v prednostni seznam onesnaževalcev okolja v Evropski unije in ZDA (*European Union Priority Pollutants List* in *U.S. Environmental Protection Agency's List*). V preglednem članku je predstavljeno trenutno poznavanje stanja ostankov triazina v vodnem okolju in njihovi strupeni učinki na ribe. Na osnovi pregleda dosedanjega poznavanja problematike smo opredelili glavne vrzeli v trenutnem znanju in nekatere usmeritve za prihodnje raziskave. Pregled vsebuje vpliv sedmih najpogostejše odkritih triazinov v vodi (ametrin, atrazin, metribuzine, prometrin, simazin, terbutilazin in terburine) na fiziologijo rib in njihovo akutno strupenost. Toksični učinki triazinov vključujejo vpliv na rast rib, njihov zgodnji razvoj, oksidativni stres in izražanje antioksidantnih encimov, pa tudi na krvne in biokemične parametre v plazmi ter na histopatološke spremembe v jetrih in ledvicah rib.

Ključne besede: triazini; ribe; strupenost; biokemični profil; hematologija; histologija