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Review

TTX accumulation in pufferfish☆

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Abstract

Tetrodotoxin (TTX) has been detected in a variety of animals. The finding of TTX in the trumpet shell *Charonia sauliae* strongly suggested that its origin was its food, a TTX-bearing starfish *Astropecten polyacanthus*. Since then, the food chain has been consistently implicated as the principal means of TTX intoxication. To identify the primary producer of TTX, intestinal bacteria isolated from several TTX-bearers were investigated for their TTX production. The results demonstrated that some of them could produce TTX. Thus the primary TTX producers in the sea are concluded to be marine bacteria. Subsequently, detritus feeders and zooplankton can be intoxicated with TTX through the food chain, or in conjunction with parasitism or symbiosis. The process followed by small carnivores, omnivores or scavengers, and by organisms higher up the food chain would result in the accumulation of higher concentrations of TTX. Finally, pufferfish at the top of the food chain are intoxicated with TTX. This hypothesis is supported by the fact that net cage and land cultures produce non-toxic pufferfish that can be made toxic by feeding with a TTX-containing diet.

Keywords: Pufferfish; Tetrodotoxin (TTX); Intestinal bacteria; Food chain; Parasitism; Symbiosis; Resistibility against TTX

Contents

1. Introduction . . . 145
2. Distribution of TTX in animals . . . 146
3. TTX producers . . . 147
4. TTX distribution in species of pufferfish . . . 147
5. TTX distribution in pufferfish bodies . . . 148
6. TTX-free pufferfish (Noguchi et al., 2004) and TTX accumulation . . . 149
7. Resistance of animals to TTX intoxication . . . 149
8. Conclusions . . . 151
Acknowledgements . . . 151
References . . . 151

1. Introduction

Until 1964 tetrodotoxin (TTX) was known to occur only in pufferfish and the question arose as to whether the TTX was of exogenous or endogenous origin. However, later, TTX was detected in many other animals (Miyazawa and

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Noguchi, 2001). In some TTX-bearing gastropods, the food was determined to be the source of the TTX (Noguchi et al., 1981, 1982). Subsequently, intestinal bacteria of TTX-bearing organisms, followed by other marine bacteria, were found to be producers of TTX (Hashimoto et al., 1990), although some were found to produce TTX in only limited quantities (Hashimoto et al., 1990; Miyazawa and Noguchi, 2001). Consequently, the main mechanism of TTX accumulation in pufferfish as being via a food web consisting of several steps, starting with marine bacteria as the primary TTX producer, was strongly favored.

To test this hypothesis, three experiments were carried out:

(1) Assess the feasibility of producing non-toxic pufferfish in net cage or land culture by preventing the invasion of TTX-bearing organisms (Noguchi et al., 2004).
(2) Determine if non-toxic pufferfish from net cage culture could be intoxicated with TTX by feeding with a TTX-containing diet (Noguchi, 1988).
(3) Elucidate the relationship between resistibility to TTX and accumulation of TTX in toxic species of pufferfish (Saito et al., 1985).

2. Distribution of TTX in animals

As mentioned above, TTX was thought to be a toxin that occurred only in pufferfish. However, since Mosher et al. (1965) detected TTX in the eggs of California newt *Taricha torosa* in 1964, the distribution of TTX has been spread

Table 1
Distribution of tetrodotoxin in animals other than pufferfish (Miyazawa and Noguchi, 2001)

Animals		Toxic parts	Maximal toxicity*	References
Platyhelminthes				
Turbellaria				
Flatworms	*Planocera* spp.	Whole body	●	Miyazawa et al. (1986)
Nemertinea				
Ribbonworms	*Lineus fuscoviridis*	Whole body	●	Miyazawa et al. (1988)
	Tubulanus punctatus	Whole body	◎	Miyazawa et al. (1988)
	Cephalothrix linearis	Whole body	●	Ali et al. (1990)
Mollusca				
Gastropoda	*Charonia sauliae*	Digestive gland	●	Narita et al. (1981)
	Babylonia japonica	Digestive gland	○	Noguchi et al. (1981)
	Tutufa lissostoma	Digestive gland	◎	Noguchi et al. (1984)
	Zeuxis siquijorensis	Whole body	●	Narita et al. (1984)
	Niotha clathrata	Whole body	●	Jeon et al. (1984)
	Natica lineata	Whole body	◎	Hwang et al. (1990)
	Cymatium echo	Digestive gland	○	Narita (1991)
	Pugilina ternotoma	Digestive gland	○	Narita (1991)
Cephalopoda	*Hapalochlaena maculosa*	Posterior salivary gland	●	Sheumack et al. (1984)
Annelida				
Polychaeta	*Pseudopolamilla occelata*	Whole body	○	Yasumoto et al. (1989)
Arthropoda				
Xanthidae crabs	*Atergatis floridus*	Whole body	○	Noguchi et al. (1983)
	Zosimus aeneus	Whole body	○	Yasumura et al. (1986)
Horseshoe crab	*Carcinoscorpius rotundicauda*	Egg	○	Kungsuwan et al. (1987)
Chaetognatha				
Arrowworms	*Parasagitta* spp.	Head	△	Thuesen et al. (1988)
	Flaccisagitta spp.	Head	△	Thuesen et al. (1988)
Echinodermata				
Starfish	*Astropecten* spp.	Whole body	◎	Maruyama et al. (1984, 1985)
Vertebrata				
Pisces				
Goby	*Yongeichthys criniger*	Skin, viscera, gonad	◎	Noguchi and Hashimoto (1973)
Amphibia				
Newts	*Taricha* spp.	Skin, egg, ovary, muscle, blood	◎	Mosher et al. (1965)
	Notophthalmus spp.	Skin, egg, ovary	◎	Yotsu et al. (1990)
	Cynopsis spp.	Skin, egg, ovary, muscle, blood	○	Yasumoto et al. (1988)
	Triturus spp.	Skin, egg, ovary, muscle, blood	△	Yotsu et al. (1990)
Frogs	*Atelopus* spp.	Skin	●	Kim et al. (1975)
	Colostethus sp.	Skin	◎	Daly et al. (1994)
	Polypedates sp.	Skin	◎	Tanu et al. (2001)

*○: 10–100 MU/g tissue (weakly toxic). ◎: 100–1000 MU/g tissue (moderately toxic); ●: >1000 MU/g tissue (strongly toxic), where 1 MU (mouse unit) is defined as the amount of toxin that kills a male mouse of ddY strain (20 g body weight) in 30 min after intraperitoneal administration. The amount is equivalent to about 0.2 μg of TTX. △: derivatives of TTX were detected (toxicity data are unavailable).