Some Carcinogenic Effects of Fungus in Livestock

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Abstract: This review focuses on Saprolegniasis in fish andthe toxicity of fumonisin B1 (FB1), a toxic metabolite of *Fusarium moniliforme*, inchickens. Saprolegniasis is the widely accepted, collective term used to describe fungal diseases of fish and fish eggs caused by members of the genera Saprolegnia, Achyla, and Dictyuchus. Historically, it has been implicated as an integral component of salmon disease. It is also sometimes referred to as fish fungus disease or fungus disease (mainly in ornamental fish) or as winter fungus/saprolegniasis when it is associated with winter kill syndrome in the channel catfish industry. Contaminated grains by fungus are considered as a source of mycotoxin in animal feeding. *Fusarium* fungi are common plant pathogens produce a toxic metabolite fumonisin B1 (FB1) which considered a causal agent of toxic effect and immunosuppression in chickens ducklings, and turkey poults and do cancer in liver of livestock.
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Introduction:

Toxic effect of Saprolegniasis in fish:

Saprolegniasis is one of the most devastating oomycete diseases in freshwater fish which is caused by species in the genus *Saprolegnia* including *Saprolegnia parasitica. (S. parasitica)* **(Shin *et al.*, 2017).** *S. parasitica* represents a serious problem in the aquaculture growth industry (**Molina *et al.* 1995; van West 2006; Phillips *et al.* 2008**). Saprolegniasis caused by *S. parasitica* affects aquaculture brood fish and incubating eggs. It is estimated that 10% of all hatched salmon succumb to saprolegniasis, causing maj or financial loss in an industry accounting for approximately 30% of the global fish production for consumption (**Molina *et al.* 1995; Murray & Peeler 2005; vanWest 2006; Fregeneda-Grandes *et al.* 2007; Phillips *et al.* 2008**).

The incidence of saprolegniasis extends to Asian tropical aquaculture systems where over 80%of fish produced by aquaculture comes from the area (**Karunasagar *et al.* 2003**). Malaysia is one of the largest producers of cultured fish, notably Seabass, through its immense expansion in cage aquaculture (**Alongi *et al.* 2002**). Though responsible for the decline in aquaculture fish populations, *S. parasitica* has also been found in natural populations of salmonids and other fresh water fish species, and it is endemic to all fresh water habitats across the globe (**van West 2006**).

Until 2002, *S. parasitica* was kept under control through the use of Malachite green; however, due to its carcinogenic and toxicological effects, treatment with this chemical has been banned internationally (**Torto-Alalibo *et al.* 2005; van West 2006; Fugelstad *et al.* 2009; Robertson *et al.* 2009**). To develop effective controls, it is necessary to better understand the molecular and physiological pathways underlying the development, pathogenicity and host specificity of saprolegniasis.

Outbreaks of *S. parasitica* infections have been significantly increased during last decade in many parts of the world after banning of organic dye, malachite green, which was the most effective anti-*Saprolegnia* agent. At present, effective control of *S. parasitica* is one of the main challenges in salmonid aquaculture. Wide array of chemicals, natural products, bacterial isolates, and UV irradiation have been researched on to find the replacement or alternative strategies for banned malachite green and to develop environmentally safe treatment methods. Anti-*Saprolegnia* agents such as formalin, boric acid, clotrimazole, potassium permanganate, copper nitrate, and copper sulfate have been tested, however, none of them have matched with the efficacy level for killing the pathogen. Few licensed anti-*Saprolegnia* agents such as pyceze and hydrogen peroxide are reported for treating salmon eggs to control *S. parasitica* infection although those agents are not very effective for high protection after hatching. Thus, identifying effective anti-*Saprolegnia* compounds can lead new avenue for sustainable control of the disease. (**Neish and Hughes, 1980; Roberts, 1989; Post, 1987; Noga, 1993; Tucker & Robinson 1990 and Meng *et al.*, 1996**).

Figure 1: Juvenile salmon infected with *S. parasitica*. The inflamed area beneath the pectoral fin indicates the area of infection (**Earle** and **Hintz, 2014**).

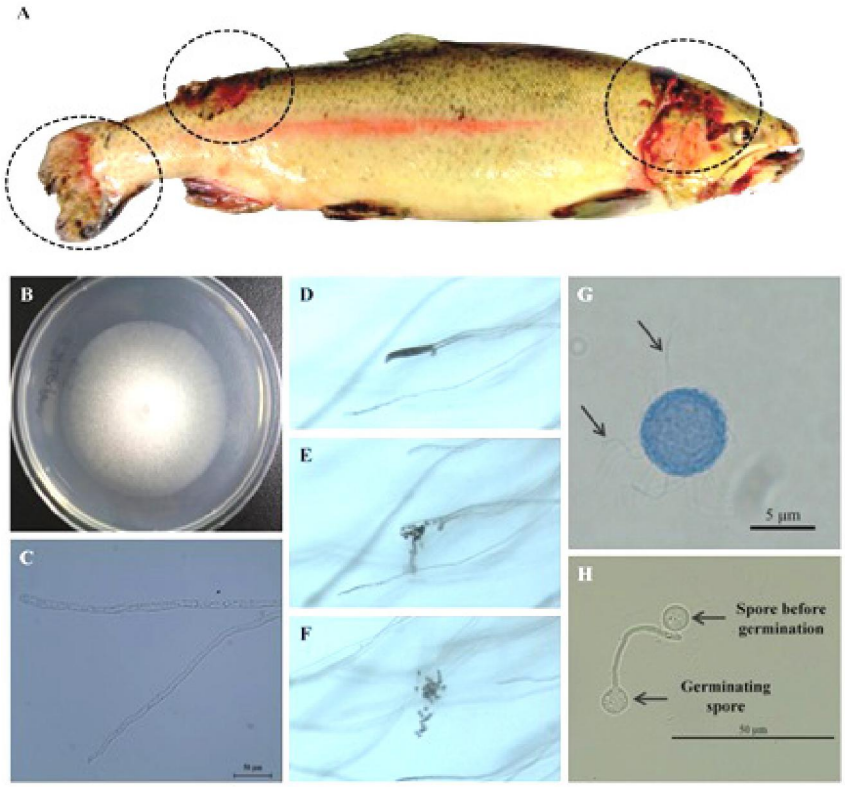

Figure 2: The morphology of *Saprolegnia parasitica* in fish. (**Shin *et al*., 2017**)

Fumonisin in chickens:

Fumonisin B1 (FB1) is a mycotoxin produced by Fusarium spp. *Fusarium moniliforme is a widespread, phytopathogenic* mold found as a contaminant on many crops, including corn, (Jeschke et al., 1987) rice, (Ogawa and Takeda, 1990) wheat (Warren and Kommedahl, 1973), barley (Hacking et al., 1976), peanut (Windingstad et al., 1989), cotton (Lagiere 1973), sorghum (Bain, 1973), and sugarcane (Moubasher et al., 1972)

When chickens, ducklings, and turkey poults fed contaminated grains by fungus the recorded symptoms were increased mortality, decreasedbody weight gain, decreased size ofthe bursa of Fabricius, thymus, and spleen, myocardial degeneration and showing hemorrhageand necrosis of hepatocytes, (Jeschke et al., 1987, Engelhardtet al., 1989). increase in the SGOT: AST ratio was reported when *F. moniliforme*-contaminated culture material containing the fumonisins was incorporated into broiler chicks diets (Ledoux et al., 1992a), Body weights and average daily gain dramatically decreased with increasing dietary fumonisin B1, and liver, proventriculus, and gizzard weights increased. Diarrhea, thymic cortical atrophy, multifocal hepatic necrosis, biliary hyperplasia, and rickets were present in chicks fed diets containing fumonisin B1. Serum calcium, cholesterol, and aspartate aminotransferase levels all increased at higher fumonisin dietary levels. Results indicate that fumonisin, from Fusarium moniliforme culture material, is toxic in young chicks. (Ledoux et al., 1992a,1992$_b$).

The mechanisms of FB1 toxicity are related to the inhibition of ceramide synthase, causing an accumulation of sphingosine (SO) and sphinganine (SA), which cause tissue functional impairment and the development of oxidative stresssubacute exposure of broiler chicks to FB1 induced liver oxidative stress concomitantly with SA/SO accumulation. (Poersch et al., 2014)

Treatment of saprolegniasis:

Treatment of the *Saprolegnia* infection is accomplished by medicating the water with potassium permanganate, after removing skin pathogens. While increased salt levels, combined with good electrolyte and calcium levels in the water, are good treatment options for an *Ichthyophonus hoferi* infection, another possible measure is raising the water temperature to 82 degrees Fahrenheit (consult a veterinarian first), as the Ichthyophonus fungi are more virulent in colder waters. It is important to thoroughly clean and sanitize the fish tank, aquarium, or fishpond for either of these injections.

Photodynamic Antimicrobial Therapy Application in Fish Farm Plants

Although just a few studies have been conducted in this field, preliminary results obtained at both laboratory level and pilot station suggest that the photochemical technique, using porphyrin derivatives as PS, has a great potential also for the disinfection of fish farming plant waters. These studies showed that cell cultures of Gram-positive bacteria (e.g., meticillin-resistant *S. aureus*), Gram-negative bacteria (e.g., *E. coli*), fungal (e.g., *C. albicans*) and fungal-like pathogens (e.g., *Saprolegnia* spp.) and parasitic protozoa (e.g., *Acanthamoeba palestinensis*) showed a 5–6 log decrease in the microbial population after 10 minutes of irradiation with low light intensities (ca. 50 mW cm^{-2}) in the presence of micromolar PS doses. Magaraggia *et al*. have also shown that a micromolar concentration of a porphyrinic PS promoted the cure of saprolegniosis in trout-farming pools containing naturally or artificially *Saprolegnia* infected fish (inactivation of 6–7 logs) without perilesional damage of the fish. A stock of fish were transferred to a 1,000 L tank and, after acclimatization, skin fish was infected by scraping dorsal trout epidermis and inoculated with *Saprolegnia* by direct contact of the lesions with mycelium wads. The infected group was dark incubated with 0.6 mg L^{-1} for 10 min in an 80–150 L pool and irradiated for 1 h kept in a closed circuit and recirculated by a motor-driven pump. The irradiation was performed by using the 400–800 nm wavelength interval emitted from two 100 W incandescent filament lamps and the water temperature was kept at 13 °C throughout the light exposure. The treatment was daily repeated for six consecutive days. After each treatment repetition, fish were moved to a 1,000 L tank. The onset of the infection in healthy fish was reduced about 50%. Recurrence of the saprolegniosis in the *Saprolegnia* infected sites or in others sites of the fish was not observed. The trout set with spontaneous infection by *Saprolegnia* a complete remission of the infection was induced within one week. The same micromolar concentrations exhibited also higher photosensitizing activity over meticillin-resistant *S. aureus* and *E. coli* (up 7 logs decrease). The antimicrobial effects of PDT were also demonstrated for *V. vulnificus* that frequently infects fish farming water. Similarly, ten bacterial species (*V. anguilarum, V. parahaemolyticus*, *Photobacterium damselae* subsp. *damselae*, *Photobacterium damselae* subsp. *piscicida*, *A. salmonicida*, *E. coli*, *Enterobacter*, *S. aureus*, *E. faecalis*, *Pseudomonas* sp.) isolated from a fish farming plant waters were effectively inactivated (up to 7 logs) *in vitro* with cationic porphyrins, at micromolar PS doses, after 90–270 minutes of irradiation with a very low light intensity of 4 mW cm^{-} showing that photodynamic therapy can be used to photoinactivate fish bacterial pathogens in fish farm waters even during dark days of winter time. In these experiments fifty milliliters of bacterial suspensions from bacterial cultures (~10^8 cells mL^{-1}) were diluted ten-fold in phosphate buffered saline to a final concentration of ~ 10^7 colony forming units mL^{-1} and exposed, in 600 mL glass beakers, to the PS under the white light. Bacterial inactivation was evaluated by counting the number of colonies, by pour plating method, in the exposed samples. (Almeida, 2009).

Irradiation of fish farming waters by solar light, which penetrates deeply into the water column,

thereby allowing the uniform illumination of large volumes makes this technology inexpensive since it is based on the use of low cost visible light sources.

The promising results of PACT on a large range of microorganisms, Gram-positive and Gram-negative bacteria including multidrug-resistant strains, bacterial spores, virus, bacteriophages, yeasts and helminths eggs and the knowledge that the porphyrins' mode of action make the selection of photoresistant strains very unlikely, suggest that this principle can be applied to photodecontamination of fish farming plants, in order to destroy pathogenic microorganisms. To implement this technology in fish farming plants some studies will be need to be carried out, namely pertaining to the determination of the stability of the new hybrid-porphyrin conjugates under visible light irradiation conditions. Moreover, there are no studies on the impact that this procedure might have on the total microbial community structure after treatment.

Prevention:

Removing dead infected fish, sanitizing the environment, and not feeding your pets raw fish are all good ways to prevent either of these fungal infections.

Recent treatment of toxins:

Probiotic lactic acid bacterium were used to reduce the effects of FB1-induced oxidative stress and organ damage in broilers. (Deepthi et al., 2017).

Novel and promising nanograde adsorbent suitable for the protection and reduction of toxicity of Fumonisin B1 via dietary inclusion of organo-modified nano-montmorillonite in rats. (El-Nekeety et al., 2017).

Electroactive nanocarbon was used as all-in-one biosensing component enables sensitive quantification of Fumonisin B_1 (FB_1) as model mycotoxin analyte, it can be easily develop label-free, cost-effective and fast bioanalytical devices for universal biosensing. (Chengand Bonanni,2018).

References:

1. Adelaide Almeida, Ângela Cunha, Newton C. M. Gomes, Eliana Alves, Liliana Costa and Maria A. F. Faustino. Phage Therapy and Photodynamic Therapy: Low Environmental Impact Approaches to Inactivate Microorganisms in Fish Farming Plants. *Marine Drugs* 2009, *7*(3), 268-313.
2. Alongi D M, Chong V C, Dixon P, Sasekumar A and Tirendi F. (2002). The influence of fish cage aquaculture on pelagic carbon flow and water chemistry in tidally dominated mangrove estuaries of peninsular Malaysia. *Marine Environmental Research* 55(4): 313–333.
3. Bain, D. C., 1973. Association of *Fusarium moniliforme* with infection of sorghum seedlings by *Sclerospora sorghi*. Phytopathology, 63:197–198.
4. Cheng ZX, and Bonanni A. (2018): All-in-One: Electroactive Nanocarbon as Simultaneous Platform and Label for Single-Step Biosensing. Chemistry. 2018 Jan 5.
5. Deepthi BV, Somashekaraiah R, Poornachandra Rao K, Deepa N, Dharanesha NK, Girish KS, Sreenivasa MY. actobacillus plantarum MYS6 Ameliorates Fumonisin B1-Induced Hepatorenal Damage in Broilers. Front Microbiol. 2017 Nov 22;8:2317.
6. Earle G, and Hintz W. New Approaches for Controlling Saprolegnia parasitica, the Causal Agent of a Devastating Fish Disease, 2014, Tropical Life Sciences Research, 25(2), 101–109, 2014.
7. El-Nekeety AA, El-Kady AA, Abdel-Wahhab KG, Hassan NS, Abdel-Wahhab MA. (2017).
8. Reduction of individual or combined toxicity of fumonisin B1 and zearalenone via dietary inclusion of organo-modified nano-montmorillonite in rats. Environ Sci Pollut Res Int. 2017 Sep;24(25):20770-20783.
9. Engelhardt, J. A., W. W. Carlton, and J. F. Tuite, 1989. Toxicity of *Fusarium moniliforme* var. *subglutinans* for chicks, ducklings and turkey poults. Avian Dis. 33:357–360.
10. Fregeneda-Grandes J M, Rodriguez-Cadenas F, Carbajal-Gonzalez M T and Aller Gancedo Fugelstad J, Bouzenzana J, Djerbi S, Guerriero G, Ezcurra I, Teeri T T, Arvestad L and Bulone V. (2009). Identification of the *cellulose synthase* genes from the Oomycete *Saprolegnia monoica* and effect of cellulose synthesis inhibitors on gene expression and enzyme activity. *Fungal Genetics and Biology* 46(10): 759–767.
11. Hacking, A., W. R. Rosser, and M. T. Dervish, 1976. Zearalenoneproducing species of *Fusarium* on barley. Ann. Appl. Biol.84:7–11.
12. Toxicon. 2018 Mar 21;146:13-23.
13. Jeschke, N., P. E. Nelson, and W. F. O. Marasas, 1987. Toxicity to ducklings of *Fusarium moniliforme* isolated from corn intended for use in poultry feed. Poultry Sci. 66:1619–1623.
14. J M. (2007). Antibody response of brown trout *Salmotrutta* injected with Pathogenic *Saprolegnia parasitica* antigenic extracts. *Diseases of Aquatic Organisms* 74(2): 107–111.
15. Karunasagar I, Karunasagar I and Otta S K. (2003). Disease problems affecting fish in tropical ecosystems. *Journal of Applied Aquaculture* 13(3–4): 231–249.
16. Lagiere, R., 1973. Cotton Boll rots in Senegal: II. Fungi isolated from boll during rot. Coton Fibres Trop. 28:493–507.

17. Ledoux, D. R., T. P. Brown, T. S. Weibking, and G. E. Rottinghaus, 1992a. Fumonisin toxicity to broiler chicks. J. Vet.
18. Diagn. Invest. 4:330–333. Ledoux, D. R., T. S. Weibking, and G. E. Rottinghaus, 1992b.
19. Effects of *Fusarium moniliforme* culture material containing known levels of fumonisin B1 on turkey poults. Poultry Sci. 71(Suppl.1):162.
20. Meng HL, Wise DJ, Robinson EH: Chemical prevention and treatment of winter Saprolegniosis ("winter kill") in channel catfish Ictalurus punctatus. J World Aquacult Soc 27(1):1-6, 1996.
21. Moubasher, A. H., M. A. Elnaghy, and S. I. Abdel-Hafez, 1972. Studies on the fungus flora of three grains in Egypt. Mycopathologia 47:261–274.
22. Molina F I, Jong S and Ma G. (1995). Molecular characterization and identification of *Saprolegnia* by restriction analysis of genes coding for ribosomal RNA. *Antonievan Leeuwenhoek* 68(1): 65–74.
23. Murray A G and Peeler E J. (2005). A framework for understanding the potential for emerging diseases in aquaculture. *Preventive Veterinary Medicine* 67(2–3): 223– 235.
24. Neish GA, Hughes GC: Fungal Diseases of Fishes. Nep- tune, NJ, TFH Publications, 1980.
25. Noga EJ: Fungal and algal disease of temperate freshwa- ter and estuarine fishes, in Stoskopf MK (ed): Fish Medicine. Philadelphia, PA, Saunders, 1993. pp 278-283.
26. Ogawa, K., and S. Takeda, 1990. Population of benomyl-resistant rice "bakanae" fungus in paddy field. Soc. Ann. Phytopathol. Ja. 56:247–24.
27. Phillips A J, Anderson V L, Robertson E J, Secombes C J and van West P. (2008). New insights into animal pathogenic oomycetes. *Trends in Microbiology* 16: 13–19.
28. Poersch AB, Trombetta F, Braga AC, Boeira SP, Oliveira MS, Dilkin P, Mallmann CA, Fighera MR, Royes LF, Oliveira MS, Furian AF. Involvement of oxidative stress in subacute toxicity induced by fumonisin B1 in broiler chicks. Vet Microbiol. 2014 Nov 7;174(1-2):180-185.
29. Post G: Textbook of Fish Health. Neptune City, NJ, TFH Publications, 1987.
30. Roberts RJ: The mycology of teleosts, in Roberts RJ (ed): Fish Pathology, 2nd edition. London, England, Baillere Tindall, 1989, pp 320-336.
31. Robertson E J, Anderson V L, Phillips A J, Secombes C J, Dieguez-Uribeondo J and van West P. (2009). *Saprolegnia* – fish interactions. In K Lamourand S Kamoun (eds.). *Oomycete genetics and genomics, diversity, interactions and researchtools*. Hoboken, NJ, USA: Wiley-Blackwell,407–424.
32. Sangyeop Shin, D. C. M. Kulatunga, S. H. S. Dananjaya, Chamilani Nikapitiya, Jehee Lee and Mahanama De Zoysa. Saprolegnia parasitica Isolated from Rainbow Trout in Korea: Characterization, Anti-Saprolegnia Activity and Host Pathogen Interaction in Zebrafish Disease Model. Mycobiology 2017 December, 45(4): 297-311.
33. Sangyeop Shin, D. C. M. Kulatunga, S. H. S. Dananjaya, Chamilani Nikapitiya, Jehee Lee, and Mahanama De Zoysa. *Saprolegnia parasitica* Isolated from Rainbow Trout in Korea: Characterization, Anti-*Saprolegnia* Activity and Host Pathogen Interaction in Zebrafish Disease Model. Mycobiology. 2017 Dec; 45(4): 297–311.
34. Torto-Alalibo T, Tian M, Gajendran K, Waugh M E, van West P and Kamoun S. (2005). Expressed sequence tags from the oomycete fish pathogen *Saprolegnia parasitica* reveal putative virulence factors. *BMC Microbiology* 5: 46. doi:10.1186/1471-2180-5-46.
35. Tucker CS, Robinson EH: Channel Catfish Farming Handbook. New York, Van Nostrand Reinhold, 1990, pp 317-380.
36. Van West P. (2006). *Saprolegnia parasitica*, an oomycete pathogen with a fishy appetite: New challenges for an old problem. *Mycologist* 20(3): 99–104.
37. Warren, H. L., and T. Kommedahl, 1973. Fertilization and wheat refuse effects on *Fusarium* species associated with wheat roots in Minnesota. Phytopathology 63:103–108.
38. Windingstad, R. M., R. J. Cole, P. E. Nelson, T. J. Roffe, R. R. George, and J. W. Dorner, 1989. *Fusarium* mycotoxins from peanuts suspected as a cause of sandhill crane mortality. J. Wild. Dis. 25:38–46.

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