

## Efficacy of fumagillin against *Thelohanellus kitauei* Infection of Israel carp, *Cyprinus carpio nudus*

Jae Ku Rhee\*, Hyeon Cheol Kim and Bae Keun Park

Department of Parasitology, School of Veterinary Medicine, Chonbuk National University  
Chonju 560-756, Korea

**Abstract:** The potential of fumagillin dicyclohexylamine salt to treat and prevent intestinal giant-cystic disease in Israel carp, *Cyprinus carpio nudus*, was monitored in field experimental studies. In experiment 1 (therapeutic), most fish were already naturally infected with more advanced stage of *Thelohanellus kitauei*. Fumagillin was administered to fish (mean body weight of 830 g) for a period of one month at a dose of 10.62 mg in the first group and 5.3 mg in the second group per fish per day. In experiment 2 (prophylactic), most fish also were already naturally infected with an early developmental stage of the protozoa and fish (average body weight of 484 g) were administered fumagillin for 45 days at a dose of 3.95 mg per fish per day. In both experiments, the cumulative mortalities of fish and the extrusion rates of the polar filaments of the spores were significantly decreased in a dose-independent fashion. In experiment 2 no dead fish were observed. No adverse side effects of the drug were observed among fish from any dosage group. In experiment 2, an oval or dot-like concave lesion of most cysts developed at the 7th day and the vegetative form was never observed at the 17th day postmedication and the cysts were grossly reduced in size as compared with the control group, beginning at the 24th day until the end of the study. In contrast, it was scarcely effective to the cysts in experiment 1. Taking the seasonal development of the protozoa into consideration, the above results revealed that oral administration of fumagillin at 3.95 mg/500 g body weight/day for a month is the optimal dose for the treatment and prevention of thelohanellosis caused by *T. kitauei* among *C. carpio nudus*.

**Key words:** *Thelohanellus kitauei*, *Cyprinus carpio nudus*, fumagillin dicyclohexylamine salt, efficacy

### INTRODUCTION

*Thelohanellus kitauei* infection of Israel carp, *Cyprinus carpio nudus*, has been one of the most serious diseases of fish in Korea since 1988. *T. kitauei* produced giant cysts on the

intestinal wall is a specific parasite of carp, the cysts usually appear at the beginning of July maturing and bursting in August and September releasing mature spores. The spores are characterized by an egg-shaped balloon-like sack,  $38.0 \pm 2.7 \mu\text{m}$  by  $15.6 \pm 1.6 \mu\text{m}$  in size on the average. The spores measure  $30.2 \pm 1.8 \mu\text{m}$  long and  $10.9 \pm 1.1 \mu\text{m}$  wide in water (Rhee *et al.*, 1990a).

In a basic attempt to develop the prophylactic and therapeutic measures of the intestinal giant-cystic disease, the course of formation and disappearance of the cysts and

• Received on Dec. 14 1992, accepted on Jan. 8 1993.

• This study was financially supported by a Grant-in-Aid for Scientific Research from the San Hak Cooperation Foundation of Korea in 1992.

\* Corresponding author

effects of physical and chemical factors on viability of the spores were reported by authors (Rhee *et al.*, 1990a & b).

Fumagillin, produced by the fungus, *Aspergillus fumigatus*, has been known to be an effective drug against myxosporeans such *Sphaerospora renicola*, *Ceratomyxa*, *Myxidium giardi*, *Thelohanelus nicolskii*, *Hofereilus carassii* and myxosporean PKX (the etiologic agent of proliferative kidney disease) that frequently cause serious disease in fish (Molnar *et al.*, 1987; Szekely *et al.*, 1988; Molnar, 1989; Yokoyama *et al.*, 1990; Wishkovsky *et al.*, 1990).

However, the efficacy of fumagillin in the treatment and prevention of the intestinal giant-cystic disease has not been investigated. The purpose of the present study was to investigate the efficacy of extended oral administration of fumagillin in the prophylaxis of the giant-cystic disease under field conditions. In addition, optimal therapeutic potential of the drug was investigated.

### MATERIALS AND METHODS

Several trials of treatment or prevention were made depending on different developmental stages of the cysts produced by *T. kitauei*. Field experiment 1 was designed for treatment of Israel carp, *C. carpio nudus*, infected with more advanced stage of *T. kitauei*. Most fish (average body weight and age of 830 g and 15 months, respectively) were already naturally infected with *T. kitauei* and showing gross signs of the disease. The small or giant cysts were observed on the intestinal mucosa. The average extrusion rate of the polar filament of the spores from the cysts was 41.2%.

A total of 1,200 fish (average total body weight of 1,000 Kg) were randomly assigned to 2 principal and control groups in the net pens (5 × 4 × 1.5 M) from a fish farm at the Soyang lake (Horim Fisheries, Chunchon-shi, Korea). Fish were fed a commercial feed (DCP; 36%) containing fumagillin at a level of 1% of their body weight each day. Fumagillin, in the form of 85% dicyclohexylamine salt (Chinoin Pharmaceutical and Chemical Works Ltd., Budapest, Hungary), was administered to fish from August 1 to August 31 at a dose of 10.62

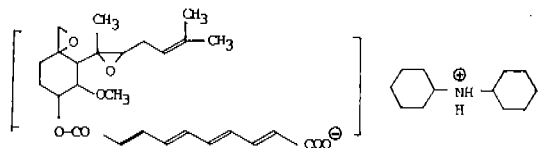
mg in the first group and 5.3 mg in the second group per fish per day as a pure ingredient. The control received feed without any drug added. Water temperature ranged from 24 to 31°C during the entire experimental period.

Field experiment 2 for prevention was carried out on fish infected with an early developmental stage of the protozoa. Most fish (average body weight and age of 484 g and 15 months, respectively) already manifested the small lesions or the small swellings on the mucosa while exhibiting no external symptoms. The average extrusion rate of the polar filament was 25.4%.

620 fish (average total body weight of 300 Kg) were randomly assigned to principal and control groups in the net pens from a fish farm at the Ocjung lake (Hyundae Fisheries, Unarm-myeon, Imsil-gun, Korea).

Fish were fed a commercial feed (DCP, 36%) containing 10% premix of fumagillin at a level of 1% total body weight per day. Fumagillin, in the form of 9.8% dicyclohexylamine salt, was administered from July 17 to August 31 at a dose of 3.95 mg per fish per day. The fumagillin-free feed used as a control diet. Water temperature ranged from 25 to 30°C during the experimental period.

In both field experiments, in order to evaluate the efficacy of the drug, the accumulative mortality of fish and the prevalence of infection were checked. Moreover, five to ten fish sampled at random from the net pens were dissected at irregular intervals in each principal and control group from the beginning the experiment until the end of the trial and measurements of the lesions or the cysts were recorded. Fresh spores were obtained from some of the cysts and were treated with 5% KOH solution to release the polar filament to assess viability. The small lesions and/or the



**Fig. 1.** Structure of fumagillin dicyclohexylamine salt, 2,4,6,8-decatetraenedioic acid [4-(1,2-epoxy-1,5-dimethyl-4-hexenyl)-5-methoxy-1-exaspiro (2, 5) oct-6-yl] monoester.

giant cysts were also processed for histopathological observations according to the method of Rhee *et al.* (1990a).

**RESULTS**

**Cumulative mortality:** In Israel carp administered with various dosages of fumagillin to different developmental stages of the disease, the cumulative mortalities of fish in both principal groups at Horiim and Hyundae Fisheries during the trial periods were significantly reduced as compared with the control groups. This effect was not dose dependent. There was no mortality in experiment 2 (Tables 1 and 2). Meanwhile, different sizes of the cysts were observed from all dead fish. No toxic side effects of any dosage of the drug were observed mac-

roscopically.

**Extrusion rate of polar filament of spore:**

The extrusion rates of the polar filament of the spores in Israel carp treated with fumagillin in both principal groups were significantly decreased in contrast with the control groups. This effect was also not dose dependent (Tables 3 and 4).

**Macro- and micro-scopical findings of cyst:**

In field experiment 1 (therapeutic), the yellowish-red small or giant cysts (4-25 mm diameter) were observed on the intestinal mucosa of most fish as a soybean-like to a quail egg-like size before medication on July 31. Histological finding revealed numerous cross sections of a single winding tubular vegetative form variable in shape and size occupying the cysts that were developed from the submucosa to the lamina propria. The

**Table 1.** Effect of fumagillin on cumulative mortality of more advanced stage of thelohanellosis in *Cyprinus carpio nudus*

Medication period; from August 1 to August 31

Groups (Dosage /fish*/day)	No. of fish exam.**	No. of dead fish	Accumul. mortality (%)
Principal First (10.62 mg)	1,200**	93	7.9
Second (5.3 mg)	1,200**	91	7.7
Control (No-drug)	1,200**	442	37.6

\* Mean body weight of 830 g.

\*\* It is excluded 27 fish from total number of each group owing to inspection.

**Table 2.** Effect of fumagillin on cumulative mortality of early developmental stage of thelohanellosis in *Cyprinus carpio nudus*

Medication period; from Junly 17 to August 31

Groups (Dosage /fish*/day)	No. of fish exam.**	No. of dead fish	Accumul. mortality (%)
Principal (3.95 mg)	620	0	0
Control (No-drug)	620	226	38.3

\* Average body weight is 484 g.

\*\* It is excluded 30 fish from total number of each group due to examination.

**Table 3.** Effect of fumagillin on extrusion rate of polar filament in more advanced stage thelohanellosis (Unit: %)

Experiment	Before	Days after medication					
		15	21	30	38	69	107
Principal							
First	41.2	21.4	15.7	15.2	14.9	13.5	12.5
Second	41.2	24.5	16.8	16.9	15.2	11.8	14.3
Control	41.2	46.8	58.0	50.7	38.2	35.5	34.3

**Table 4.** Effect of fumagillin on extrusion rate of polar filament in early developmental stage thelohanellosis

(Unit: %)

Experiment	Before	Days after medication						
		7	17	24	29	36	43	50
Principal	25.4	13.5	20.3	28.8	27.2	26.7	22.5	16.0
Control	25.4	31.8	35.7	39.2	58.7	52.4	46.7	42.0

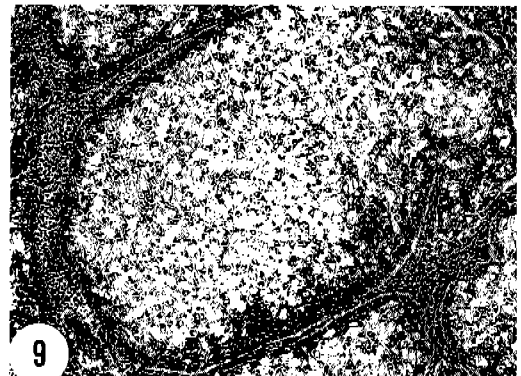
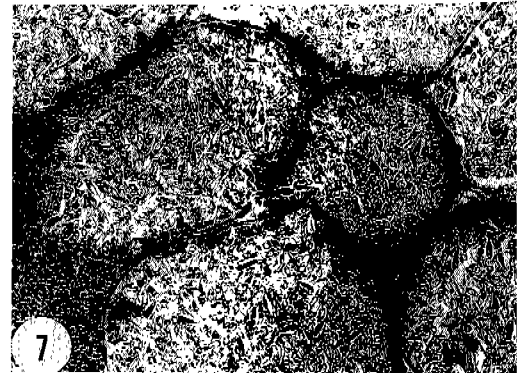
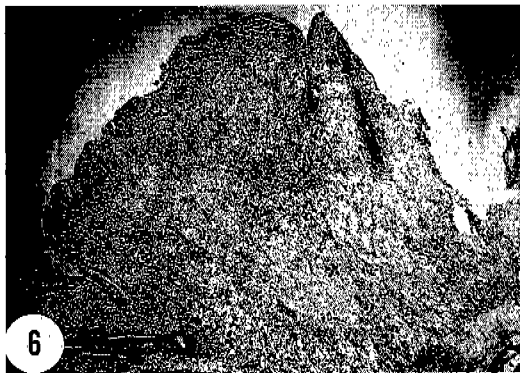
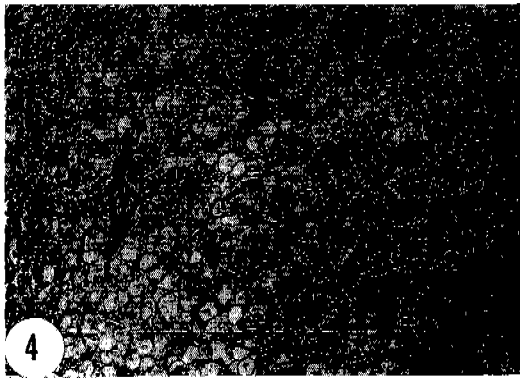
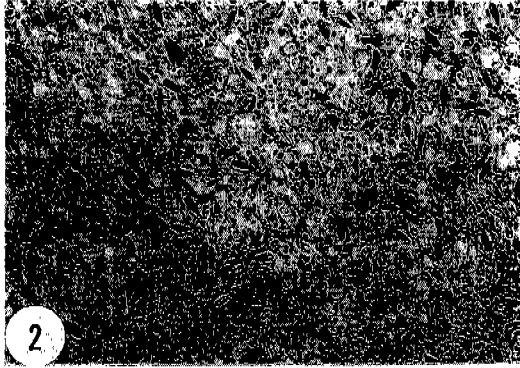
small cysts were filled with immature spores, while the large cysts contained mature spores. Granular wandering cells were revealed in the interstitium among the cross sections in the cysts. Newly formed capillaries were also recognized in the giant cysts.

On the 15th day after medication (August 15), treated fish in the first group (fumagillin 10.62 mg/fish/day) had spherical cysts (7.6 × 10.4 mm average size) on the mucosa. An oval concave lesion (3.5 mm average diameter) in central portions of most cysts was apparent (Fig.10). In many cases, autolysis *i.e.* vanishment of the cross sections, had already occurred leaving free spores and their debris uniformly scattered in the lesions (Fig. 2). Also, an aggregate of the small vacuoles containing the debris of the spores or no one was surrounded by some granular wandering cells and numerous lymphocytes. When an oval concave lesion was not observed, the small or large cross sections including a few mature spores and their debris were visible in

the cyst. In the instance that fish were not feeding due to severe thelohanellosis, an oval concave lesion of the cysts (17.5 × 23.0 mm average size) was not shown, but a lot of the cross sections were usually revealed. In the second group (5.3 mg fumagillin/fish/day), gross and histologic alterations of the cysts were very similar to those observed in group 1.

On the other hand, a number of pleomorphic cysts (10.5 × 12.1 mm average size) developed on the mucosa, and inner part of the cysts was filled up with the cross sections in the control group. Mature spores and their debris were observed throughout about 600 cross sections (50 × 150-50 × 350 μm size) examined. The interstitium among the cross sections infiltrated by granular wandering cells and numerous lymphocytes with moderate proliferation of connective tissue. The thick encapsulation of the cysts was composed of new or old connective tissue and intestinal columnar epithelium. The intestinal mucosa was partially desquamated by the cyst (Fig. 3).

**Figs. 2-9.** Light micrographs showing sections of the cysts produced by *Thelohanellus kitauei* on the intestinal mucosa of Israel carp, stained with H & E. **Fig. 2.** Free spores and their debris uniformly scattered in the lesion. 15 days post-treatment (August 15) in group 1 of experiment 1, × 400. **Fig. 3.** A number of the cross sections with mature spores and their debris. 15 days post-drug-free feeding (August 15) in experimental 1, × 200. **Fig. 4.** An aggregate of the small vacuoles is visible and granular wandering cells and lymphocytes are infiltrated. 107 days post-treatment (November 15) in group 1 of experiment 1, × 400. **Fig. 5.** Some cross sections of highly degenerated vegetative form are replaced with massive hyperplastic connective tissue in a lesion during the healing process. 107 days post-non-drug feeding (November 15) in experiment 1, × 200. **Fig. 6.** The lesion is filled with filamentous connective tissue, some mature spores and their debris, granular wandering cells and lymphocytes. 24 days post-treatment (August 9) in experiment 2, × 80. **Fig. 7.** The cross sections are filled up with mature spores, and granular wandering cells and lymphocytes have accumulated in the interstitium among the cross sections. 24 days post-non-drug feeding (August 9) in experiment 2, × 400. **Fig. 8.** Mature spores, granular wandering cells and lymphocytes are visible in the lesions. 43 days post-treatment (August 28) in experiment 2, × 400. **Fig. 9.** Partially ruptured vegetative form and the spores in the interstitium among the cross section and throughout the section are visible. Notice the distribution of granular wandering cells and lymphocytes in peripheral portions of the walls of the vegetative form and the interstitium. 43 days post-non-drug feeding (August 28) in experiment 2, × 400.



On day 30 after medication (August 30), the sizes of the cysts of the first group were measured at 5-15 (8.3) × 5.5-25 (10.8) mm. Each oval concave lesion of the cysts measured 4 mm average diameter. The muscular layer of the intestine was completely ruptured, causing the cyst to slightly protrude to the serosa in most cases. In general, the cross sections were not revealed from the cysts, however, mature spores and granular wandering cells were widely distributed and lymphocytes were very numerous in several parts of the cyst. Loose connective tissue was moderately proliferated. In contrast, no cells of the mucosal epidermis were seen. In group two, alterations of the macro- and micro-scopic findings were very similar to those of the first group. On the other hand, the finding of the cyst in the control group were similar to those of the 15th day after non-drug feeding.

On day 69 after treatment (October 8), the cysts of 6-10 mm in diameter were detected on the mucosa in the first group. A part of the cysts was projected to the serosa, and the cysts were ruptured at the top. Some traces of the small and large cross sections were discovered, and a few mature spores, their debris and the small vacuoles remained in the inner segments. Additionally, a few free mature spores and the small vacuoles bordering the edge were observed. There was peripheral infiltration characterized by granular wandering cells and numerous lymphocytes. The epithelial layer of the mucosa had degenerated and was partially desquamated. In the second group, a convex lesion (2 mm diameter) was observed on the mucosa and granulated tissue of identical size as the lesion from the submucosa of the section surface. Other finding were similar to those of the first group.

In the control group, yellowish-white or pink cysts (15-20 × 20-32 mm size) were observed. The section surface was soft and a large quantity of whitish abscess-like material was seen at the surface. A number of the cross sections were variable in shape and size. Other finding were very similar to those observed in previous drug-free feeding group.

On day 107 (November 15), white convex lesions, of approximately 2 mm in diameter,

were observed on the intestinal mucosa of the first group and the section surface contained round granulated tissue of approximately 1 mm in diameter. A mass of vacuoles (375-450 × 500-625 μm size) were observed with a few of the spores remaining intact. Lesions demonstrated loose connective tissue proliferation with pronounced infiltration of granular wandering cells and lymphocytes. However, epithelial cells of the mucosa were desquamated (Fig. 4). In the second group, round white lesions, 3-4 mm in diameter, were observed. The large and small cross sections (12.5-750 × 225-1375 μm size) revealed insertion of loose connective tissue and a few mature spores, their debris and the small vacuoles from the interior.

In the control group, the cysts were ruptured at the apex, probably due to the pressure caused by mature spores. The cysts had the appearance of a ripe pomegranate and the cross sections were fused by bursting with the periphery frequently unrecognizable. Some cross sections of highly degenerated vegetative form were replaced with massive hyperplastic connective tissue, while a decreased number of mature spores, numerous lymphocytes and granular wandering cells were found inside and outside the cross sections of the lesions during the healing process (Fig. 5).

Field experiment 2 (prophylactic), before treatment (July 16), demonstrated the small, not swelled visible lesions or the small swellings (1-4.1 mm diameter) on the intestinal mucosa from most fish observed as a poppy seed to pimple like body. In paraffin section of the swellings, many cross sections of a single winding tubular vegetative form were prominently manifested with a few mature spores.

On day 7 following treatment (July 23), most fish had the small yellowish-white lesions (1 mm diameter) or oval to spherical cysts (4-6 mm diameter) on the intestinal mucosa, each containing a dot-like concave lesion appearing in the center. Many cross section (187.5 × 262.4 μm average size) had distribution of more mature spores. The cross sections were surrounded by granular wandering cells and lymphocytes.

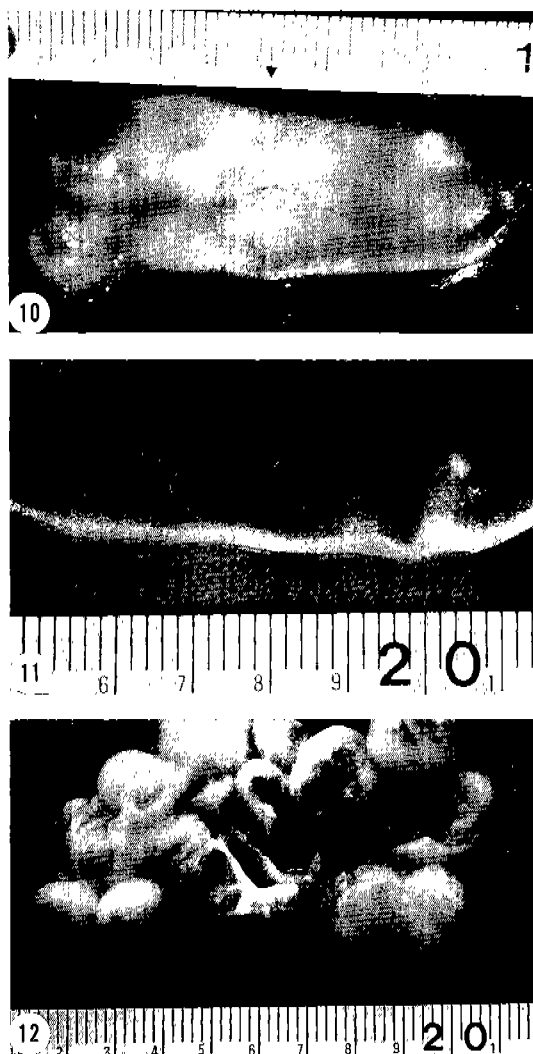
On day 17 following treatment (August 2),

the small yellowish-white cysts with a concave central lesion (2-3 mm diameter) on the mucosa were obtained from most fish. The tissues had autolysed in most cases leaving an even distribution of free spores.

On day 24 following treatment (August 9), most fish were observed with the small yellowish-white swellings (2.61 mm average diameter) on the mucosa with a concave central lesion. No walls of a single winding tubular vegetative form were observed. The swellings were filled with filamentous connective tissue, some mature spores and their debris, granular wandering cells and lymphocytes (Fig. 6). On the other hand, spherical red and white cysts (1.76 × 2.21 cm average size) were not affected in the control group. The cross sections (296.3 × 436.2 μm average size) were filled with mature spores, and insertion of granular wandering cells and lymphocytes had occurred in the interstitium among the sections (Fig. 7).

Day 29 following treatment (August 14) observed spherical white cysts (2.86 × 2.86 mm average size) with no mature spores and with a concave lesion in the center. The lesions contained granular wandering cells and lymphocytes. Whereas, spherical pink to red cysts (2.17 × 2.39 cm average size) were observed in the control group.

On day 43 following treatment (August 28), the small yellowish-white cysts were observed (Fig. 11). Histological findings were similar to those at day 29, except for sparsely distributed mature spores in the lesions (Fig. 8). In the control group spherical reddish-white cysts (2.27 × 2.73 cm average size) with a rupture at the apex were observed (Fig. 12). The cross sections were packed with mature spores. Walls of the cross sections were partially ruptured, and the spores were seen in every field of intra- and extra-cross sections (271.7 × 463.4 μm average size). In addition, infiltration of connective tissue was noted in the interstitium and the interior. Granular wandering cells and lymphocytes were observed in peripheral portions of the walls and the interstitium (Fig. 9).



**Figs. 10-12.** Photographs showing the cysts produced *T. kitauei* on the intestinal mucosa of Israel carp. **Fig. 10.** Note an oval concave lesion in the center of each of the cysts. 15 days post-treatment (August 15) in the first group of experiment 1. **Fig. 11.** Small yellowish-white swellings. 43 days post-treatment (August 28) in experiment 2. **Fig. 12.** Spherical cysts are ruptured at the apex. 43 days post-drug-free feeding (August 28) in experiment 2.

## DISCUSSION

These data represent the first attempt to use chemotherapeutically and prophylactically fumagillin against naturally occurring the intestinal giant-cystic disease of Israel carp.

These data indicate that fumagillin in the diet is the most effective means of reducing the incidence of the disease. Light microscopy examination of treated fish revealed sporocidal activity, destruction of a single winding tubular vegetative form and formation of a large number of the small vacuoles. Mortality of fish, prevalence of infection and survival and viability of the spores were also monitored.

The mechanism of the action of fumagillin has not been defined. In microsporeans, Hartwig and Przelecka (1971) reported the drug suppressed DNA synthesis of *Nosema apis*, while Jaronski (1972) reported RNA synthesis inhibition of *Octosporea muscaedomesticae*. Yokoyama *et al.* (1990) indicated that the drug has hoferelloidal action rather than hoferellostatic action in *Hoferellus carassii*, a myxosporean, in goldfish, *Carassius auratus*. This study revealed destruction of the vegetative form and death or decrease of viability of the spores at an early phase shortly after treatment. This suggests a thelohanelloidal action rather than a thelohanellostatic action.

It is suggested that the efficacy and the administration period of the drug is dependent on the stage of the infection. Fish which were infected but apparently normal at the beginning of July were completely prevented from developing the disease and no mortality was observed with following fumagillin treatment (3.95 mg/484 g average body weight/day for one month) in experiment 2. Fish with gross signs of the disease did not recover completely.

Toxicity of fumagillin was shown by Sitja and Alvarez (1989). They observed that fumagillin-treated sea bass, *Dicentrarchus labrax*, infected with *Sphaerospora testicularis* manifested side effects. Wishkovsky *et al.* (1990) noted that rainbow trout, *Oncorhynchus mykiss*, fed 0.5 and 1.0 g fumagillin/kg in feed exhibited side effects beginning 4 weeks after medication. The spleen and kidney of fish administered the higher dose of the drug were grossly reduced in size. Microscopic examinations revealed a decrease in the amount of interstitial hematopoietic tissue in the anterior and posterior kidney and splenic lymphoid tissue. In contrast, Kano *et al.* (1982) and Yokoyama

*et al.* (1990) did not observe any fumagillin-related abnormalities in Japanese eel, *Anguilla japonica* and goldfish. Our studies are consistent with the studies of Kano *et al.* (1982) and Yokoyama *et al.* (1990). This was probably due to the low dosage used (3.95 mg/484 g average body weight/day).

We conclude that fumagillin has significant thelohanelloidal action and that extended oral administration at 3.95 mg/500 g body weight/day for a period of one month, before development of the disease, i.e. at the beginning of July, seems to be the most effective form of treatment.

#### ACKNOWLEDGEMENTS

We extend our appreciation to Horim Fisheries, Chunchon-shi and Hyundae Fisheries, Imsil-gun, Korea, for kindly supplying the fish and to Chinoin Pharmaceutical and Chemical Works Ltd., Budapest, Hungary, for kindly providing the fumagillin.

#### REFERENCES

- Hartwig A, Przelecka A (1971) Nucleic acids in intestine of *Apis mellifica* infected with *Nosema apis* and treated with fumagillin DCH; Cytochemical and autoradiographic studies. *J Invert Pathol* **18**: 331-336.
- Jaronski ST (1972) Cytochemical evidence for RNA synthesis inhibition by fumagillin. *J Antibiotics* **25**: 327-331.
- Kano T, Okauchi T, Fukui H (1982) Studies on *Pleistophora* infection in eel, *Anguilla japonica*. II. Preliminary tests for application of fumagillin. *Fish Pathol* **17**: 107-114 (in Japanese).
- Molnar K, Baska F, Szekely C (1987) Fumagillin, an efficacious drug against renal sphaerosporosis of the common carp, *Cyprinus carpio*. *Dis Aquat Org* **2**: 187-190.
- Molnar K (1989) Possible uses of fumagillin against different fish parasites. Chinoin Pharmaceutical and Chemical Works Ltd. Budapest, Hungary p1-4.
- Rhee JK, Kim JO, Kim PG, Park BK (1990a) Prophylactic and therapeutic studies on intestinal giant-cystic disease of the Israel carp caused by *Thelohanellus kitauei*. I. Course of formation and vanishment of the cyst. *Korean J Parasit* **28**(3): 183-194.



Rhee JK, Kim JO, Park BK (1990b) Prophylactic and therapeutic studies on intestinal giant-cystic disease of the Israel carp caused by *Thelohanellus kitauei* II. Effects of physical and chemical factors on *T. kitauei* spores *in vitro*. *Korean J Parasit* **28**(4): 241-252.

Sitja-Bobadilla A, Alvarez-Pellitero P (1989) *Int Conf Eur Ass Fish Pathol* 24-28. Sep., Spain p195.

Szekely C, Molnar K, Baska F (1988) Efficacy of fumagillin against *Myxidium giardi* Cepede, 1906 infection of the European eel (*Anguilla anguilla*): New observations on myxidiosis of imported glass eels. *Acta Veterinaria Hungarica* **36**(3-4): 239-246.

Wishkovsky A, Groff JM, Lauren DJ, Toth RJ, Hedrick RP (1990) Efficacy of fumagillin against proliferative kidney disease and its toxic side effects in rainbow trout (*Oncorhynchus mykiss*) fingerlings. *Fish Pathol* **25**(3): 141-146.

Yokoyama H, Ogawa K, Wakabayashi H (1990) Chemotherapy with fumagillin and toltrazuril against kidney enlargement disease of goldfish caused by the myxosporean *Hoferellus carassii*. *Fish Pathol* **25**(3): 157-163.

=국문초록=

### 향어의 장포자충증에 대한 Fumagillin의 예방 및 치료 효과시험

전북대학교 수의과대학 기생충학교실

이재구 · 김현철 · 박배근

향어의 장포자충증을 예방, 치료하기 위한 일환으로 fumagillin의 효과시험을 야외에서 수행하였다. 실험 1(치료)에서는 장포자충증의 종류가 중등도로 형성된 향어(평균체중 830 g)를 3군으로 나누어 가두리에 사육하였다. 하루에 처음 군은 10.62 mg, 두번째 군은 5.3 mg의 fumagillin을 8월 1일부터 한달동안 사료에 혼합하여 부여하였으며 세번째 군은 대조로 하였다. 실험 2(예방)에서는 장포자충증이 초기상태인 향어(평균체중 484 g)를 2군으로 나누어 가두리에 사육하였다. 처음 군에는 하루에 3.95 mg의 fumagillin을 7월 17일부터 45일 동안 역시 사료에 혼합하여 부여하였으며 다음 군은 대조로 하였다. 두 실험에서 향어의 누적 폐사율과 포자의 극사탈출율은 약제농도의 차이에 관계없이 대조군에 비하여 모두 유의있게 감소하였다. 약제에 의한 부작용은 전혀 관찰할 수 없었으며, 특히 실험 2에서 폐사어는 전혀 인정할 수 없었다. 약제 투여후 실험 1의 15일째와 실험 2의 7일째에 대부분 종류의 중앙부에 하나의 난원형 또는 작은 점 비슷한 함몰부가 형성되었으며, 실험 1의 15일째와 실험 2의 17일째에는 관상영양형의 횡단면이 전혀 인정되지 않았다. 실험 2의 24일째와 실험 1의 30일째에 있어서 종류의 조직학적 소견은 치유과정을 취하고 있었으며, 실험 2의 경우 24일 이후에는 종류의 크기가 대조에 비하여 모두 현저하게 작았다. 이상의 실험결과로 미루어 보아 장포자충증을 예방, 치료하기 위하여 종류가 형성되기 전인 7월 상순에 체중 500 g 향어에 매일 3.95 mg의 fumagillin을 한달동안 경구투여하는 것이 가장 효과적이라고 하겠다.

(기생충학잡지 31(1): 57-65, 1993년 3월)