

**EFFECT OF FLUMEQUINE ON GROWTH AND CHROMOSOMES
OF NILE TILAPIA (*OREOCHROMES NILOTICUS*)**

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ABSTRACT

The present study aimed to investigate the effect of flumequine on growth of Nile tilapia when used as prophylactic and chemotherapeutic agent in both aquarium (tanks) and concrete ponds as well as its cytogenetic effect, the present study was carried out as two experiments. In the first experiment, the fish were reared in glass tanks, using fingerlings of monosex Nile tilapia (all male sex reversal). Fish were grouped into four groups (in two replication) groups 1 served as control, fish in groups 2 were administered therapeutic dose 12 mg/kg of body weight/day, as medicated feed for successive 5 days, groups 3 were administered subtherapeutic dose 10 mg/kg of body weight/day during the experimental period (9 weeks) and groups 4 were administered 6 mg / kg of body weight/day during the experimental period. Growth parameters, feed conversion ratio, protein efficiency ratio, and survival rate were recorded. Flumequine residues in tissue were determined as well as cytogenetic studies were performed. The second experiment was carried out in a fish farm. Fish were reared in concrete ponds. One-month age monosex fry were used. Fry were divided into two groups, first group (control) was fed control diet free from flumequine. The second group was fed medicated diet, flumequine was added at dose of 10-mg/kg of body weight/day during incubation period, then the two groups were fed control basal ration until the end of experiment. The following results were obtained, flumequine in dose of 10 mg / kg of body weight/day caused a significant increase in the body weight, weight gain and protein efficiency ratio, in addition to improvement in feed conversion ratio, compared with control group reared in glass tanks (experiment I). Survival rate found to be 89.30, 85.72, 100 and

92.86% for fish groups fed the experimental diets 1, 2, 3 and 4, respectively. Flumequine in dose of 10 mg/kg of body weight/day caused significant increase in chromosomal aberration, compared with control group. Flumequine residues were detected in fish tissue until 10 days after last feeding in group administered 10 mg/kg of body weight/day, whereas fish administered 6 mg/kg of body weight/day, flumequine not detected after 10 days of last feeding. Addition of flumequine to fish diets at dose of 10 mg/kg of body weight/day in concrete ponds (Experiment II) caused significant decrease in body weight at the end of incubation period, this decrease became non significant at the end experiment. From the obtained results it could be concluded that, flumequine in dose of 10 mg/kg of body weight/day caused significant increase in growth rate, and improved feed conversion ratio as well as increased in survival rate in aquarium system. However, in fish farm flumequine caused inhibition of growth rate. Subsequently, flumequine in dose of 10 mg/kg of body weight/day can be used as prophylactic dose in aquarium system as tanks for improvement of growth and decrease mortality especially during incubation period.

INTRODUCTION

Flumequine is a “second generation” antibacterial quinolone derivative, structurally related to nalidixic acid and oxolinic acid, and is active against a wide range of Gram-negative bacteria (Edelson et al., 1977; Neuman 1978 and Lemeland et al., 1981). Quinolones also active against fungi, protozoan and helminthes (Rogstad et al. 1993). The use of antibacterial has been introduced into a fish farm both to treat and to prevent infectious diseases which considering the high stocking density of this kind of farming are steadily increasing (Malvisi et al. 1994). Moreover, the last decade quinolones have been administered routinely to cultured fish in many countries both as a prophylactic and as chemotherapeutic agent (Austin et al. 1983; Rodgers and Austin 1983 and Austin, and Austin 1987). However, Heijden et al., (1995) reported that flumequine possesses mitogenic properties in Europeans eels. Accordingly, the aim of the present study is to evaluate the effect of the flumequine on the growth of Nile tilapia when used as prophylactic and chemotherapeutic agent in both aquarium (tanks) and concrete ponds farm as well as its cytogenetic effect.

MATERIALS AND METHODS

The present study was carried out as two experiments; experiment I, and Experiment II.

Experiment I:

First experiment of the present study was conducted at the laboratory of Aquaculture Research, Faculty of Agriculture at Moshtohor, Zagazig University. Fingerlings of Nile tilapia were obtained from Abbassa hatchery, Sharkya Governate. The experimental fish were transported in plastic bags filled with water and oxygen to the fish laboratory. Fish were adapted and distributed randomly into 8 glass tanks. The fish were weighed and the initial weight for each aquarium was recorded. Each aquarium was stocked with fourteen fish.

Fish grouping: Fish were grouped into four groups and arranged in two replicates.

Group (1): control groups kept without treatment.

Group (2): administered therapeutic dose 12 mg/kg of body weight/day given as medicated feed for 5 days, (Malvisi et al., 1994), after 5 days fish were fed a control fish diet.

Group (3): administered subtherapeutic dose 10 mg/kg of body weight/day as medicated feed for all the experimental period.

Group (4): administered subtherapeutic dose 6 mg/kg of body weight/day as medicated feed for all experiments period.

Aquarium system: Eight glass aquarium 100 ×40×50 cm. Each aquarium was filtered with bio- mechanical filter. Air was bubbled by 2 air stones connected to an air pump in each aquarium. Water temperature was kept at $28 \pm 1^{\circ}\text{C}$.

Fish diets: the diets were composed of fishmeal, soybean, yellow corn, wheat flour, wheat bran, oil, mineral mixture, and vitamins. The diets containing $31 \pm 0.5\%$ protein and 10% lipid. Fish were given the diets at a daily rate 3% of total biomass. Fish were fed twice daily at 9 a.m. and 3 p.m.

All fish groups were initially weighed and at 3, 6, and 9 weeks. Growth performance (live body weight, weight gain and specific growth rate) were calculated. Feed conversion ratio (feed dry matter/weight gain) and protein efficiency ratio (weight gain/protein ingested) were calculated.

Determination of flumequine in tissues:

Flumequine residues in liver and in muscle and skin were determined at the end of the experiment (24 hours after the last feeding), then after 10, 20 days of the last feeding. During this period all fish groups feed on basal control diet free from flumequine.

Flumequine assay:

Concentration of flumequine in tissues were done microbiologically by a hole-plate modification of agar diffusion method (Nouws and Ziv, 1976) using Mueller –Hirton agar adjusted to pH 6.0 and a locally isolated E-coli strain as a test organism. Sensitivity limit of the assay method was 0.15 ug/ml.

Effect of flumequine on survival rate:

The mortality rate was recorded in all groups during all experimental period. Then survival ratio was calculated.

Cytogenetic studies:

Chromosomal Preparation: At the end of experiment, 4 fish from each tank were used for cytogenetic studies. Each fish was injected 0.05% colchicine intraperitoneally, 3 hr before sacrificed. Mitotic chromosomes then were obtained from kidney tissue according to method described by **Al-Sabti et al., (1983)**. From each fish, 50 well spread metaphase were examined for kidney cells and different types of chromosomal abnormalities were recorded such as structural aberrations including chromatid breaks, chromatid gaps, fragment deletion, centromeric attenuation and centric fusion.

Experiment. II:

This experiment was carried out in Aqua Omam Fish farm at Sadat City. In this experiment fish were reared in concrete ponds supplied with groundwater. One month age monosex Nile tilapia fry were obtained from

Al-Abbasa hatchery were used in this experiment. During incubation period (45 days), 6,000 fry were reared in two concrete tanks, about 3,000 fry were reared in each tank. The volume of each tank was 100 m³. Fish were fed starter commercial ration powder containing 40% protein. The first fish group (control group) was fed basal commercial diet powder (fishmeal, soybean, yellow corn wheat flour, wheat bran oil, mineral mixture and vitamins), the second fish group flumequine was added to the ration powder at dose of 10mg/kg of body weight/day. In both groups fish were fed 3% of its weight. About 1/3 of water in each tank was changed every 3days.

During growing period (3 months) fish were reared in concrete tanks (100m³). 300 fish from each group were reared in tank at density 3 fish/ m³. Both two groups were fed basal growing ration (fishmeal, soybean, yellow corn wheat flour, wheat bran oil, mineral mixture and vitamins) The diet containing 25% protein and 10% lipid containing no flumequine.

One hundred fry were initially weighed from both groups and the mean body weight was recorded. At the end of incubation period 100 fish from each group were weighed. Also at the end of fattening period 100 fish were weighed.

Statistical analysis:

The statistical analysis of data was carried out by applying the computer program, SAS (1996).

RESULTS

1- Effect of flumequine on body growth.

Experiment I:

Table 1 showed the effect of flumequine on body weight and survival rate, it revealed that flumequine at therapeutic dose (12 mg/kg of body weight/day for 5 successive day) caused non significant increase in body weight after 3, 6 weeks from the experimental start, whereas after 9 weeks there was non significant decrease compared with control group.

While flumequine at dose of 10mg/kg of body weight/day caused significant increase in body weight at the experimental periods 3, 6 and 9 weeks compared with control group, flumequine at dose of 6 mg/ kg of body weight/day caused significant increase in body weight at 3 and 9 weeks but at 6 weeks caused non significant increase compared with control group.

Survival rate found to be 89.30, 85.72, 100 and 92.86% for fish groups fed the experimental diets 1, 2, 3 and 4, respectively indicating the improvement of survival rate when flumequine was added to tilapia diets at a dose of 10 mg/kg of body weight/day.

Table 2 showed that effect of flumequine on specific growth rate, it revealed that flumequine at therapeutic dose caused non significant decrease during all experimental period compared with control group, whereas flumequine at dose of 10 and 6 mg /kg of body weight/day caused non significant increase compared with control group.

Table 3 showed the effect of flumequine on weight gain, it revealed that flumequine at therapeutic dose caused significant decrease in weight gain, whereas flumequine at dose of 10 and 6 mg/kg of body weight/day caused significant increase in weight gain compared with control group.

Table 4 demonstrated the effect of flumequine on feed conversion ratio, it revealed, flumequine at dose of 10 and 6 mg/kg of body weight/day caused improvement in feed conversion ratio, where as therapeutic dose caused non significant change in feed conversion ratio compared with control group.

Table 5 Showed the effect of flumequine on protein efficiency ratio. Results in this table revealed that ratio, flumequine at dose of 10 mg/kg of body weight/day caused significant increase in protein efficiency ratio, whereas flumequine in dose of 6 mg/kg of body weight/day caused non significant increase. However, therapeutic dose caused non significant decrease compared with control group.

Cytogenetic studies:

Table 6 showed that, flumequine in dose of 10 mg/kg b.w. caused

significant increase in total chromosomal aberrations compared with control group, whereas the other treatments caused non significant increase in total chromosomal aberrations. Chromosomal breaks and deletion were also significantly increased in fish administered flumequine at dose 10 mg/kg of body weight/day compared with control group.

Flumequine residues:

Flumequine was not detected in fish administered 12 mg/kg of body weight/day for 5 days (table7) whereas as fish administered 10 mg/kg of body weight/day flumequine was detected in liver and muscles at 24 hr, 10 days and 20 days after the last feeding. While fish administered mg/kg of body weight/day, flumequine was detected in liver and muscles at 24hr, 10 days and not detected after 20 days (table 7).

Experiment II:

Table 8 Showed effect of flumequine on growth of fish in concrete ponds it revealed that flumequine caused significant decrease in the body weight during the incubation period, then this decrease became non significant at the and of the fattening cycle.

Table (1): Least squares means and standard error for the effect of Flumequine levels on body weight (g) of Nile tilapia *O. niloticus*.

Treatment	Body weight (g)					Survival rate
	No. of Fish	Initial	3.weeks	6weeks	9 weeks	
Group1	28	8.61±0.43 a	13.75±0.70 c	20.89±1.14 b	26.70±1.11 b	89.30
Group2	28	8.53±0.43 a	14.53±0.70 bc	21.35±1.14 ab	25.43±1.11 b	85.62
Group3	28	8.89±0.43 a	16.64±0.70 a	24.59±1.14 a	32.95±1.11 a	0.00
Group4	28	8.58±0.43 a	16.09±0.70 ab	23.82±1.14 ab	30.41±1.11 a	92.86

Table (2): Least squares means and standard error for the effect of Flumequine levels on specific growth rate of Nile tilapia *O. niloticus*.

Treatment	0-3 weeks	3-6 weeks	6-9 weeks	0-9 weeks
Group1	2.22±0.09 b	1.99±0.11 a	1.17±0.09 ab	1.80±0.10 a
Group2	2.53±0.09 b	1.83±0.11 a	0.83±0.09 b	1.73±0.10 a
Group3	2.99±0.09 a	1.87±0.11 a	1.40±0.09 a	2.08±0.10 a
Group4	2.99±0.09 a	1.87±0.11 a	1.16±0.09 ab	2.01±0.10 a

Means with the same letters in each column are not significantly different (P<0.05).

Table (3): Least squares means and standard error for the effect of Flumequine levels on weigh gain (g) of Nile tilapia *O. niloticus*.

Treatment	0-3 weeks	3-6 weeks	6-9 weeks	0-9 weeks
Group1	5.14±0.10 c	7.14±0.10 b	5.81±0.29 c	18.09±0.10 c
Group2	6.10±0.10 b	6.92±0.10 b	4.18±0.29 d	12.59±0.10 d
Group3	7.75±0.10 a	7.95±0.10 a	8.36±0.29 a	24.06±0.10 a
Group4	7.51±0.10 a	7.73±0.10 a	6.59±0.29 a	21.83±0.10 b

Table (4): Least squares means and standard error for the effect of Flumequine levels on feed conversion ratio of Nile tilapia *O. niloticus*.

Treatment	0-3 weeks	3-6 weeks	6-9 weeks	0-9 weeks
Group1	1.76±0.10a	2.02±0.09a	3.77±0.06b	2.51±0.10a
Group2	1.51±0.10ab	2.12±0.09a	5.78±0.06a	2.69±0.10a
Group3	1.17±0.10b	1.82±0.09a	2.62±0.06d	1.89±0.10b
Group4	1.20±0.10b	1.87±0.09a	3.28±0.06c	2.08±0.10b

Table (5): Least squares means and standard errors for the effect of Flumequine levels on protein efficiency ratio of Nile tilapia *O. niloticus*.

Treatment	0-3 weeks	3-6 weeks	6-9 weeks	0-9 weeks
Group1	1.90±0.03 b	1.65±0.03 a	0.88±0.03 ab	1.33±0.03 b
Group2	2.21±0.03 b	1.57±0.03 a	0.62±0.03 b	1.24±0.03 b
Group3	2.86±0.03 a	1.84±0.03 a	1.27±0.03 a	1.77±0.03 a
Group4	2.77±0.03 a	1.88±0.03 a	1.00±0.03 ab	1.60±0.03 ab

Table (6): Effect of flumequine on chromosomes of Nile tilapia *O. niloticus*.

Treat.	No.	Br	Gaps	Frag	Del	C.A	CF	Total
Group1	8	0.50 b	0.50 a	0.25 a	0.50 b	1.00 a	0.50 a	3.00 b
Group2	8	0.25 b	0.50 a	0.50 a	0.75 b	1.75 a	0.50 a	4.00 b
Group3	8	2.00 a	0.86 a	0.43 a	3.71 a	1.14 a	0.71a	8.86 a
Group4	8	0.60 b	0.63 a	0.25 a	0.88 b	1.38 a	0.63 a	4.25 b
S.E.		±0.29	± 0.25	±0.18	±0.43	±0.34	±0.26	±0.61

Means with the same letters in each column are not significantly different (P<0.05).

Br.: (chromatid breaks) Gaps.: (chromatid gaps) Frag.: (chromatid fragment)
 Del.: (deletion) C.A.: (centromeric attenuation) C.F.: (centromeric fusion)
 No. : number of samples

Table (7): Flumequine concentration in tissues (liver & muscle and spleen).

Fish groups	Concentration (ug/g)					
	24 hr after the last feeding		10 days after last feeding		20 days after last feeding	
	Liver	Muscles & skin	Liver	Muscle & skin	Liver	Muscle & skin
Group (1)	0	0	0	0	0	0
Group (2)	0	0	0	0	0	0
Group (3)	13.85±0.18	5.21±0.002	3.52±0.31	2.94±0.05	0.31±0.01	0.83±0.01
Group (4)	4.35±0.13	2.31±0.001	0.77±0.002	0.41±0.01	0	0

Table (8): Least squares means and standard error for the effect of Flumequine on body weight of Nile tilapia in fish farm.

Treatment	Initial weight (Mean weight)	Body weight and of incubation period (Mean ± S.E)	Body weight at the end of experiment (Mean ± S.E)
Control group	0.68	9.98 ± 0.32 a	149.10 ± 1.96 a
Flumequine administered group	0.85	8.05 ± 0.25 b	147.95 ± 1.15 a

Means with the same letters in each column are not significantly different (P<0.05).

DISCUSSION

The present study showed that using of flumequine of 10 mg/kg of body weight/day (subtherapeutic dose) in glass aquarium caused significant increase in body weight, weight gain without significant increase in specific growth rate, whereas smaller dose (6mg/kg of body weight/day) caused significant increase this observed increase in body weight and weight gain caused by using medicated feed containing flumequine could be attributed to improved conversion ratio and increased protein efficiency as observed in this study. Generally, Antimicrobial compounds are used as growth promoters in livestock, (**Brander et al. 1993**). Moreover these compounds can improve growth rate and feed conversion efficiency by preventing diseases and

maintaining health in animals in an environment likely to reduced performance due to the increased incidence of disease (**Brander et al., 1993**) moreover, flumequine has been used in intensive fish farm to treat many fish diseases such as furunculosis (**Scallan and Smith 1995**), in addition to its broad spectrum activity particularly against Gram-negative bacteria, as well as fungi, protozoans and helminths (**Rogstad,1993**). However, **Moutou et al (2001)** reported that using flumequine as medicated diet in rainbow trout caused decrease in specific growth rate. The latter attributed this result to decreased palatability. In contrast, **Elema et al. (1994)** observed no palatability problems or reduction in appetite were evident in Atlantic salmon fed on medicated diet containing flumequine.

The effect of flumequine on growth seems to be depend on dose and duration of treatment as well as method of rearing of fish. In the present study, the experiment II (fish farm) fish fed a diet containing flumequine in dose of 10 mg/kg of body weight/day caused significant decrease in body weight during incubation period. This result is contrary to the obtained results in glass aquaria in experiment I. Thereby method of rearing of fish seems to be the cause of the observed different results in this study. The observed inhibitory effect of flumequine on growth of fish in concrete ponds (fish farm) could be attributed to inhibitory effect of flumequine on growth of algae in the concrete ponds (**Lutzhof et al. 1999**). Because algae has important biological role in the fish environment in the concrete ponds. They considered as a source of oxygen and also have nutritionalrole as they help to nitrogen fixation.

Using of flumequine in this study as medicated diet in glass aquaria caused significant decrease in the mortality rate and increased survival ratio. This could be attributed to preventing disease and maintaining health in fish because flumequine has wide range of antibacterial and antifungal activities (**Rogstad, 1993**) which might be decreased mortality rate.

The elimination rate of antibacterial compounds in fish is closely linked to several factors, the most important of which is water temperature (Sohlberg et al. 1990). Also, Hansen et al. (2000) observed noticeable differences between species. In the present study, elimination rate of flumequine from tissues (muscle & liver) was also affected by the concentration of flumequine in the diet, at which flumequine was detected in small amount in both muscle and liver up to 20 days after last feeding in group administered 10 mg/kg of body weight/day, while fish administered 6 mg/kg of body weight/day, flumequine was not detected after 20 days after last feeding. Administration of therapeutic dose (12 mg/kg of body weight/day) for 5 successive days, flumequine was not detected in tissues (liver & muscle) at the end of experiment (after 9 weeks). Hansen et al. (2000) found that elimination of flumequine from eel was slow compared to turbot and halibut. In orally administered eels substantial amounts of flumequine remained in all major organs and tissues for 7 days, at 28 days significant levels of flumequine were present in liver, kidneys, and skin (with trace in muscle), whereas in orally administered turbot, significant levels of flumequine were observed over 96 h in bile, urine, skin, and bone and traces were detected over 28 days in bone, eye, and bile. Moreover, Sohlberg et al. (1994) reported that flumequine levels were detected in the plasma of rainbow trout reared at 13°C 21 days after oral administration. However, Malvisi et al. (1994) found that flumequine residues in edible tissues (muscle) was present up to 120 hr after end of medication, the latter attributed this differences to method of extraction and/or by possible differences in rearing conditions.

In this study, screening of the frequency of chromosomal damage was evaluated by using chromosomal observation in kidney cells. The present study showed that high dose of flumequine (10 mg/kg of body weight/day) has induced significant increase in chromosomal aberrations when compared with control group. In the same aspect, a number of reports have indicated on adverse effect of flumequine on fish and animals Heijden et al. 1995, Yoshida et al. (1999).

The recorded chromosomal aberrations obtained by flumequine might be attributed to the inhibition of DNA synthesis, DNA repair mechanisms or both. Since DNA is the primary target for the induction of chromosomal damage (**Obe et al 1982**) which arises as consequence of misrepair or misreplication of the damaged DNA (**Evans, 1977**) The obtained results showed that the chromosomal aberrations induced by flumequine were significantly decreased after interruption of medication in therapeutic dose (12 mg/kg of body weight/day). These results indicate that chromosomal aberration induced by flumequine might be recovered by interruption of medication.

We recommended that addition of flumequine in dose of 10 mg/kg of body weight/day as prophylactic dose at fish diet reared in aquarium system increases growth rate and decreases mortality. Fish reared on the medicated feed containing flumequine must be reared on diet free from flumequine for 30 days at least before human consumption to avoid flumequine residues in tissues.

REFERENCES

- Al-Sabti, k.; Fiag, N. and kurelec, R. (1983):** A simple and fast technique for chromosome preparation in fish. *Vet. Arh.*, 54: 83-89.
- Austin, B. and Austin, D.A. (1987):** Control of bacterial fish diseases. In: *Bacterial Fish Pathogens: Disease in Farmed and wild Fish*. Ellis Horwood, Chichester, PP.331-353.
- Austin. B., Rayment, J. and Alderman, D.J. (1983):** Control of furunculosis by oxolinic acids. *Aquaculture*, 31:101-108.
- Brander, G.C. Pugh, D.M., Bywater, R.J. and Jenkins, W.L (1993):** *Veterinary Applied Pharmacology and Therapeutics*, Bailliere Tindall, 5th Ed. PP 289-290.
- Edelson, J., Davidson, C. and Benziger, D. P. (1977):** Quinolone and Anaquino lone antimicrobial agents. *Drug Metabolism Reviews*,

6:105 – 148.

- Elema, M. O., Hoff, K.A. and Kristenesen, H.G. (1994):** Multiple-dose pharmacokinetic study of flumequine in Atlantic salmon (*Salmo salar* L.) Aquaculture 128 1-11.
- Evans H.J (1977):** Molecular mechanisms in the induction of chromosomal aberrations. In progress in Genetic Toxicology (Edited by Scott D., Bridges B.A. and Sobels F.H.), Elsevier/ North Holland, Amsterdam pp. 57-74.
- Hansen, M. K. Ingebrigtsen, K., Hayton, W. L. and Horsberg, T. E. (2001):** Disposition of ¹⁴C-flumequine in eel, *Anguilla anguilla*, turbot scorphthalmus maximus and halibut Hippoglossus hippoglossus after oral and intravenous administration. Dis Aquat Organ 47(3) : 183 –91.
- Heijden M.H., Booms G. H., Tanck, M., Rombout J. H. and Boon J. H. (1995):** Influence of flumequine on in vivo mitogen responses of European eel (*Anguilla anguilla*, lymphoid cells. Vet Immunol. Immunopathol, 47: 1.43-52.
- Lemeland, J.F., Roger, J.P.H. and Hubert, G. (1981):** Les nouvelles quinolones. Revue Medicine (Paris), 22:121-126.
- Lutzhoft, H.H., Halling - Sorensen, B. and Jorgensen, S.E. (1999): Algal toxicity of antibacterial agents applied in Danish fish farming. Arch. Environ. Contam. Toxicol, 36 (1) : 1-6.
- Malvisi J., Giorgetti, G., Raspa M., Giuliani, A., Tomasi, L. and Roncada, P. (1994):** Kinetics of flumequine in rainbow trout (*Oncorhynchus mykiss*). Rivista Italiana Acquacoltura, 29:121-128.
- Moutou, K.A., Mcarty, I.D. and Houlihan, D.F. (2001):** Effect of dietary flumequine on food consumption and growth in rainbow trout. Aquaculture International 9:95-102.
- Neuman, M. (1978):** flumequine Drugs of Today, 14:365-366.

- Nouws, J.P.M. and Ziv,G.(1976):** The effect of storage at 4°C on antibiotic residues in kidney and meat tissues of dairy cows. Tijdschrift voor Diergenees Kiende, 101: 1145-1153.
- Obe G. Natarajan A.T. and Pahtti F., (1982):** Role of DNA double-Strand breaks in the formation of radiation induced chromosomal aberrations. Prog. Mutat. Res. 4, 1-9.
- Rodgers, C. J. and Austin, B. (1983):** Oxolinic acid for control of enteric red-mouth disease in rainbow trout. Vet. Rec., 112-83.
- Rogstad, A., Ellingsen, O. F. and Syversen, C. (1993):** Pharmacokinetics and bioavailability of flumequine and oxolinic acid after various routes of administration to Atlantic salmon in seawater. Aquaculture, 110 : 207 – 220
- SAS (1996):** SAS Procedure Guide “version 6.12 Ed” . SAS Institute Inc., Cary, NC, USA.
- Scallan, A. and Smith, P.R. (1995):** Control of asymptomatic carriage of *Aeromonas salmonicida* in Atlantic salmon smolts with flumequine. In: Fish and Shellfish Pathology (ed. A.E. Ellis), Academic Press, London.
- Sohlberg. S. Aulie, A. and Soli N.E. (1994):** Temperature dependent absorption and elimination of flumequine in rainbow trout (*Oncorhynchus mykiss*) in fresh water Aquaculture, 19:1-10
- Sohlberg, S., Czerwinska, K., Rasmussen, K and Soli, N.E. (1990):** Plasma concentration of flumequine after intra-arterial and oral administration to rainbow trout (*Salmo gairdneri*) exposed to low water temperatures. Aquaculture. 84 : 355-361.
- Yoshida, M., Miyajima, k., Shiraki, K; and Kudoh, k., Nakae, P., Takahashi, M. and Maekawa, A.(1999):** Hepatotoxicity and consequently increased cell proliferation are associated with flumequine hepatocarcinogenesis in mice. Concer lett 141 (1-2) : 99 – 107.

تأثير الفليموكوين على النمو والكروموسوماتفى أسماك البلطى النيلي

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3- قسم بيولوجيا الخلية بالمركز القومى للبحوث.

استهدف البحث دراسة تأثير الفليموكوين على النمو فى سمك البلطى النيلي عند استخدامه فى الوقاية

أو العلاج سواء فى الأحواض الزجاجية أو فى المزارع السمكية، بالإضافة إلى دراسة تأثيره السيتوجينى. أجرى البحث فى تجربتين: التجربة الأولى تم إجراؤها على إصبعيات البلطى النيلي وحيد الجنس فى أحواض زجاجية. تم تقسيم الأسماك إلى أربع مجموعات (كل مجموعة فى مكررين) المجموعة الأولى كانت مجموعة ضابطة والمجموعة الثانية أعطيت جرعة علاجية من الفليموكوين ١٢ ملجرام/ كيلو جرام من وزن الاسماك لمدة خمسة أيام متتالية مع العليقة. المجموعة الثالثة والرابعة تم اعطائها جرعة تحت علاجية ١٠ و ٦ ملجرام / كيلو جرام من وزن الأسماك على الترتيب ولمد ٩ أسابيع.

وقد تم تسجيل مقاييس النمو ومعامل التحويل الغذائى ومعامل كفاءة البروتين بالإضافة إلى نسبة الحيوية فى السمك معدل النفوق كما تم تعيين متغيرات الفليموكوين وأيضاً دراسة التأثيرات الخلوية الوراثية.

أما التجربة الثانية فقد تم إجرائها فى مزرعة سمكية مفتوحة حيث تم تحضين زريعة الأسماك فى أحواض أسمنتيه. ثم تم تقسيم الزريعة إلى مجموعتين، المجموعة الأولى ضابطة وأعطيت عليقة خالية من الفليموكوين والمجموعة الثانية أعطيت عليقة محتوية على الفليموكوين بنسبة ١٠ ملجرام/ كيلوجرام من وزن السمك فى خلال فترة التحضين ثم تم إعطاء كلا المجموعتين عليقة خالية من الفليموكوين حتى نهاية التجربة.

وكان من أهم النتائج التى تم الحصول عليها ما يلى:

- عند إعطاء جرعة الفليموكوين ١٠ ملجرام/ كيلوجرام من وزن الأسماك/يوم نتج عنه زيادة معنوية فى الوزن وزيادة فى معامل كفاءة البروتين بالإضافة إلى التحسن فى معامل التحويل الغذائى بالمقارنة بالمجموعة الضابطة فى الأحواض الزجاجية (التجربة الأولى).

- كانت نسبة الحيوية للأسماك ٨٩,٣٠ % ، ٨٥,٧٢ % ، ١٠٠ % ، و ٩٢,٨٦ % فى المجموع ١ ، ٢ ، ٣ ، ٤ على التوالى.

- استخدام الفليموكوين بجرعة ١٠ ملجرام/ كيلوجرام من وزن الأسماك/يوم أحدث زيادة معنوية فى تشوهات الكروموسومات بالمقارنة بالمجموعة الضابطة.

- أوضحت النتائج وجود متغيرات للفليموكوين فى أنسجة الأسماك حتى اليوم العشرين بعد آخر جرعة فى الغذاء وذلك بالنسبة لمجموعة الأسماك المعاملة الثالثة (١٠ ملجرام/ كيلوجرام من وزن السمك)، كما ظهرت متغيرات للفليموكوين فى المجموعة التى أعطيت ٦ ملجرام/ كيلوجرام من وزن الأسماك/يوم وذلك بعد مرور ١٠ أيام وإختفت آثار الفليموكوين من أنسجة أسماك هذه المجموعة بعد مرور ٢٠ يوم من آخر معاملة غذائية.

- أدت إضافة الفليموكوين إلى عليقة السمك بجرعة ١٠ ملجرام/ كيلوجرام من وزن السمك فى المزرعة السمكية إلى حدوث نقص معنوى فى وزن الجسم عند نهاية فترة التحضين، لكن هذا النقص أصبح غير معنوياً عند نهاية التجربة.

من نتائج البحث نستخلص ما يلى: أن استعمال الفليموكوين بنسبة ١٠ ملجرام/ كيلوجرام من وزن السمك/يوم يحسن من مقاييس النمو ويقلل من نسبة النفوق فى الأحواض الزجاجية. كما يمكن استعمال الفليموكوين بنفس النسبة فى الأحواض الخرسانية المفتوحة فى الوقاية من الأمراض وتقليل نسبة النفوق خصوصاً أثناء فترة التحضين.