

## PHARMACOKINETICS AND *IN VITRO* EFFICACY OF FLORFENICOL IN EUROPEAN SEABASS (*Dicentrarchus labrax*)

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### Introduction

Florfenicol (FLO) is a synthetic amphenicol antibiotic that exerts broad spectrum antibacterial activity against Gram-negative bacilli, gram-positive cocci and other atypical bacteria. Moreover, FLO is a highly lipophilic drug providing thus high concentrations to treat intracellular pathogens. The pertinent literature on the use of FLU in aquaculture indicates that the drug has promising properties in fish. In this study, the absorption and depletion of FLO in European seabass following a multiple oral dosing, were investigated. Minimum inhibitory concentration tests (MIC) were also carried out against some important bacterial pathogens of European seabass.

### Materials and methods

European seabass kept at 24°C, received a medicated diet with FLO (10 mg/kg fish) for 7 consecutive days. Blood samples were taken from 10 individuals in each time point from 2 to 24 hours and days 2, 3, 4, 5, 6 and 7. Following the completion of the treatment, 10 fish were killed and muscle plus skin samples were obtained for 5 consecutive days. An HPLC method with fluorescence detection was used for FLO measurements in plasma and muscle samples of individual fish at each time point. The MIC values of FLO were also determined for bacterial fish pathogens isolated from diseased European seabass in Greece including *Aeromonas veronii* *bv sobria*, *Vibrio anguillarum* strain, *V. harveyi*, *Photobacterium damsela* subsp. *damsela*, *P. damsela* subsp. *piscicida* and *Edwardsiella anguillarum*.

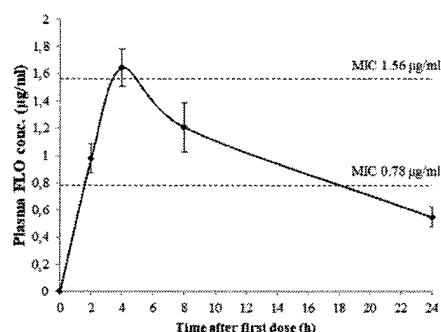


Fig. 1. Mean plasma concentrations of FLO (10mg/kg fish) during first treatment day.

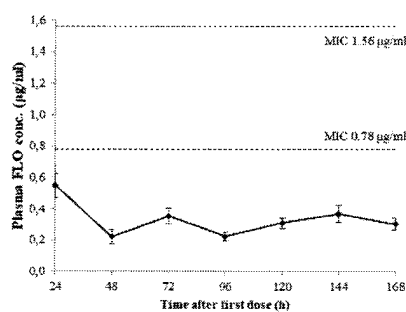


Fig. 2. Minimum plasma concentrations of FLO after multiple oral administrations at 10 mg/kg per day for seven consecutive days.

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## Results

Maximum plasma concentrations of FLO in European seabass revealed values around 1.5 µg/ml at 4h post feeding during the first day (Fig.1), while during the seven-day therapy, mean plasma concentrations of FLO showed no statistical differences between 24h time intervals (Fig. 2).

Based on the muscle plus skin FLO levels (including the amine), withdrawal times for FLO were calculated to be less than 3 days post treatment. The MIC values of FLO were measured to be 0.78 µg/ml for *A. veronii* by *sobria*, *P. damsela* subsp. *piscicida* and *E. anguillarum* and 1.56 µg/ml for *V. anguillarum*, *V. harveyi* and *P. damsela* subsp. *damsela*. Based on the MIC values alone, none of the tested strains can be considered as resistant to FLO in the current trial.

## Conclusions

FLO is readily absorbed and rapidly eliminated from European seabass edible tissues. A PK/PD evaluation of FLO properties as a time-dependent bacteriostatic antibacterial, fits to a predictive model of  $T_c > MIC$  where  $T_c$  is the percentage of the inter-dosing interval during which the serum/plasma concentration exceeds the *in vitro* MIC against the target bacterium. Considering the above model, FLO could be a potentially efficient 'off label' antibacterial against some bacterial pathogens of European seabass tested herein. A double FLO dosing, administered twice a day may aid to obtain higher circulatory daily drug levels in European seabass, but this remains to be experimentally verified.

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