# TEMPERATURE AND DOSE-DEPENDENT METABOLISM OF FLORFENICOL IN TILAPIA: PATHWAYS TO FLORFENICOL AMINE

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## Introduction

Florfenicol (FF) is a broad-spectrum antibiotic widely used in aquaculture to treat bacterial infections [1]. It has two reported primary metabolic pathways in terrestrial animals: an oxidative route through florfenicol alcohol (FFOH) and a reductive path potentially involving florfenicol monochloride (FFCL); both have the final product florfenicol amine (FFA). These processes diversify the metabolic profile of FF and influence its pharmacokinetics behavior [2]. Interspecies variations in metabolic enzymes can lead to differences in FF metabolism between aquatic and terrestrial animals, impacting drug efficacy and residue levels. Understanding the metabolic pathways and influencing factors in is essential for improving therapeutic applications in aquaculture and mitigating the risks of antibiotic residues in the environment.

## Materials and Methods

Tilapia (400- 500 g) reared at 25 ℃ & 30 ℃

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FF oral administration at a recommended dose of 10 and 15 mg/kg for 5 days

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**Homogenize Tilapia liver and skin/muscle**
0.5 g tissue was extracted by acetonitrile (ACN) containing 1% acetic acid, followed by injection to LC-MS/MS for identification of FF metabolites

## Results

TABLE 1: Concentrations (μg/g) of FF and its metabolites following 10 mg/kg FF administration for 5 days at 25˚C (n=5).

**DAY 5 10 mg/kg/day at 25°C**

| Analytes | skin/muscle | Liver |
|---|---|---|
| **FF** | 5.8 ± 0.4 | 0.4 ± 0.5 |
| **FFOH** | 2.7 ± 0.3 | 1.4 ± 0.2 |
| **FFCl** | nd. | nd. |
| **FFA** | 1.2 ± 0.3 | 0.7 ± 0.1 |

TABLE 2: Concentration (μg/g) of FF and its metabolites following 10 mg/kg FF administration for 5 days at 30˚C (n=5).

**DAY 5 10 mg/kg/day at 30°C**

| Analytes | skin/muscle | Liver |
|---|---|---|
| **FF** | 3.9 ± 0.2 | 0.6 ± 0.4 |
| **FFOH** | 3.0 ± 0.5 | 0.8 ± 0.1 |
| **FFCl** | nd. | nd. |
| **FFA** | 1.3 ± 0.3 | 0.5 ± 0.2 |

TABLE 3: Concentrations (μg/g) of FF and its metabolites on day 1 and 5 following 15 mg/kg/day for 5 days at 30°C (n=5).

**DAY 1 15 mg/kg/day at 30°C**

| Analytes | skin/muscle | Liver |
|---|---|---|
| **FF** | 3.6 ± 0.1 | 0.2 ± 0.2 |
| **FFOH** | 1.5 ± 0.1 | 1.6 ± 1.2 |
| **FFCl** | nd. | nd. |
| **FFA** | 0.8 ± 0.03 | 0.7 ± 0.2 |

**DAY 5 15 mg/kg/day at 30°C**

| Analytes | skin/muscle | Liver |
|---|---|---|
| **FF** | 4.6 ± 1.9 | 0.2 ± 0.2 |
| **FFOH** | 6.0 ± 0.5 | 1.6 ± 1.2 |
| **FFCl** | nd. | nd. |
| **FFA** | 2.9 ± 0.4 | 0.7 ± 0.2 |

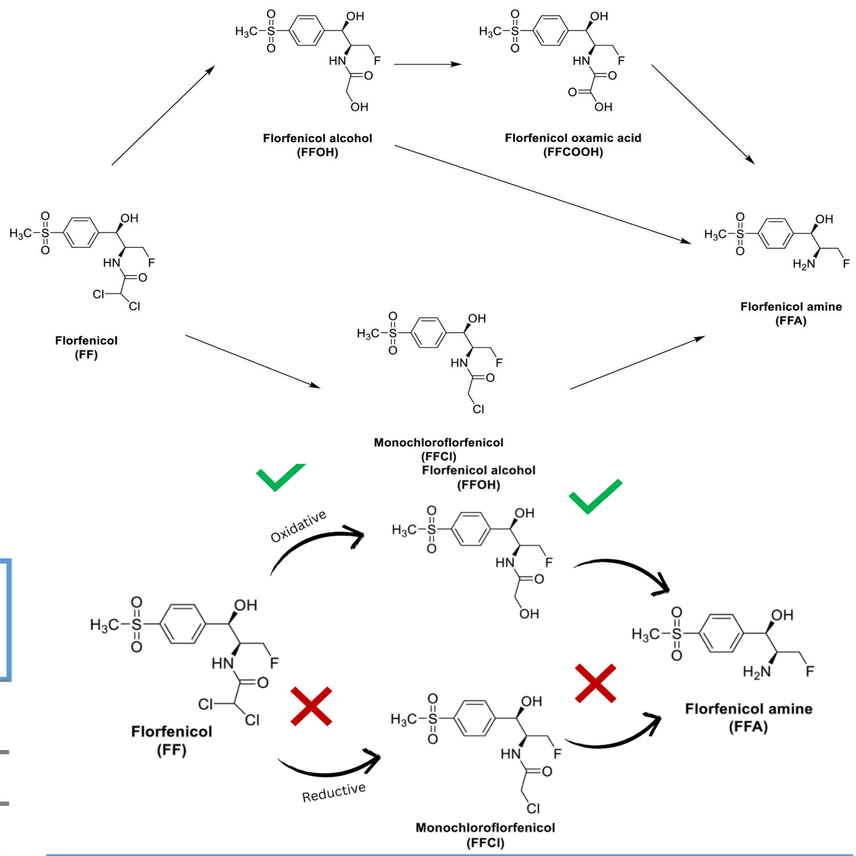


Figure 1. Proposed metabolic pathway of FF in terrestrial animal (Anadón et al. [2]) and Nile Tilapia (lower panel).

## Conclusion

- In tilapia, florfenicol (FF) metabolism primarily follows the oxidative pathway through florfenicol alcohol (FFOH) to florfenicol amine (FFA).
- Higher concentrations of FF are found in skin/muscle compared to the liver, indicating rapid hepatic conversion and tissue deposition.
- Day 1 and Day 5 (15 mg/kg/day, 30°C) agreed with the assumption that FFOH being the most prominent intermediate, maintaining a FFOH/FFA ratio of 2 throughout the process.
- Elevated water temperature (30°C) accelerates metabolic process of FF to FFOH.
- The absence of detectable FFCL suggests the reductive pathway plays a minor role.
- **These findings highlight the primary metabolic route of FF in Tilapia/fish and the significant influence of temperature on its metabolism**.

## References

1. Yang, F., et al., Pharmacokinetics of florfenicol and its metabolite florfenicol amine in crucian carp (*Carassius auratus*) at three temperatures after single oral administration. *Aquaculture*, 2019. 503: p. 446-451.
2. Anadón, A., et al., Plasma and Tissue Depletion of Florfenicol and Florfenicol-amine in Chickens. *Journal of Agricultural and Food Chemistry*, 2008. 56(22): p. 11049-11056.

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