

**Title:** Identification of a novel androgen receptor agonist (or “androgen mimic”) of environmental concern: spironolactone

**Authors:**

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**Abstract:**

Spironolactone is a pharmaceutical that acts as an androgen receptor (AR) antagonist in humans to treat certain conditions such as hirsutism, various dermatologic afflictions, and female pattern hair loss. The drug is also used to treat hypertension as a diuretic. With this common usage in humans it is conceivable that spironolactone could enter aquatic environments, and indeed has been detected downstream of a pharmaceutical manufacturer. Predictive methods to analyze human AR orthology suggest that vertebrates would be highly sensitive to chemicals that target the AR compared to invertebrate species. As a means to assess the predictive nature of molecular target orthology leading to unintended effects, 21-d reproduction studies were conducted with two fish species, *Pimephales promelas* (fathead minnow) and *Oryzias latipes* (Japanese medaka) and the invertebrate *Daphnia magna*. Spironolactone significantly reduced fecundity of medaka and fathead minnows at test concentrations of 50 and 5 µg/L, respectively, whereas *Daphnia* reproduction was not affected at 500 µg/L. Masculinization of females of both fish species was observed at 5 µg/L and 0.5 µg/L as evidenced by development of papillary complexes on medaka and tubercle formation on fathead minnows, respectively. Effects in fish occurred at concentrations below those reported in the environment. These results suggest that species with greater orthology to the human AR are susceptible to spironolactone. Further, this drug has the potential to affect reproduction in fish and should be included in environmental monitoring for contaminants of emerging concern. *The contents of this abstract neither constitute nor reflect official US EPA policy.*

**Keywords:** fathead minnow, medaka, daphnia, masculinization

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I prefer platform presentation

<b>STICs Field</b>	<b>Entry</b>
1 – Influence/profile	Not applicable
2 – Clearance tracking no.	Assigned automatically
3 – Principal Investigator / Project Officer	Carlie Lalone
4- Product title	Copy and paste from abstract
5 - Authors	See abstract All e-mail addresses in EPA system
6a- Product type	Presentations and technical summaries
6b-Product subtype	Abstract
6c – Records schedule	Not a senior official
7a – Impact statement	n/a
7b- Product description	Paste in abstract
8 – Bibliographic citation	SETAC North America 33rd Annual Meeting, 11-15 November, Long Beach, CA, USA.
9 - Access	Public
10 – Tracking and Planning Task	2.1.1 2.1.1: Adverse outcome pathway (AOP) discovery and definition
10 – Tracking and Planning Product	(2) AOP descriptions comparing linkages (e.g., causal) between specific pathway perturbations and reproductive or developmental outcomes in multiple species (e.g., rodents, fish, invertebrates) (reports). These will provide data that support the development of tools and guidance cross-species extrapolation of effects and hazard.
11 – Copyright permission	No
12 - QA	not applicable
13 – Policy implications	No
14 - Keywords	adverse outcome pathway species comparison pharmaceuticals reproduction