

## Accepted Manuscript

Title: Low-dose metformin exposure causes changes in expression of endocrine disruption-associated genes

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PII: S0166-445X(17)30354-5

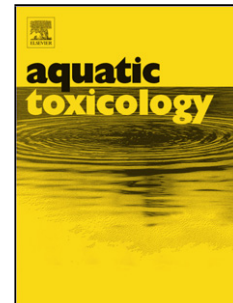
DOI: <https://doi.org/10.1016/j.aquatox.2017.12.003>

Reference: AQTOX 4815

To appear in: *Aquatic Toxicology*

Received date: 5-12-2017

Accepted date: 7-12-2017



Please cite this article as: Niemuth, Nicholas J., Klaper, Rebecca D., Low-dose metformin exposure causes changes in expression of endocrine disruption-associated genes. *Aquatic Toxicology* <https://doi.org/10.1016/j.aquatox.2017.12.003>

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## **Low-dose metformin exposure causes changes in expression of endocrine disruption-associated genes**

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### **Abstract**

The presence of intersex fish in watersheds around the world is a warning of the presence of anthropogenic endocrine-disrupting compounds (EDCs) being deposited into the aquatic environment. The anti-diabetic drug metformin is among the most prevalent and ubiquitous of the myriad pharmaceuticals found in wastewater effluent and watersheds worldwide. In addition to its prescription for type-2 diabetes, metformin is indicated as a treatment in cancers and the endocrine disorder polycystic ovarian syndrome (PCOS). Our previous research found evidence of endocrine-disruption following *Pimephales promelas* (fathead minnow) exposure to metformin at an environmentally relevant concentration. However, the mechanism of action leading to these impacts is unknown. Although metformin does not structurally resemble classical EDCs, there's an increasing recognition that endocrine disruption may occur by mechanisms other than classical endocrine receptor binding, and metformin's off-label use for treating endocrine-related disorders such as PCOS indicates its potential interaction with the endocrine system. To further explore metformin's mechanism of action as an EDC, we measured

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