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Transcriptome and physiological effects of toxaphene on the liver-gonad reproductive axis in male and female largemouth bass (Micropterus salmoides)

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ABSTRACT

Toxaphene is an organochlorine pesticide and environmental contaminant that is concerning due to its atmospheric transport and persistence in soil. In Florida, toxaphene and other organochlorine pesticides were used heavily in agriculture on the north shore of Lake Apopka and they are still detectable in soil. Wild largemouth bass that inhabit the lake and the marshes along the north shore have been exposed to a variety of organochlorine pesticides including dieldrin, methoxychlor, and p,p′-DDE, among others. While these other organochlorine pesticides have been studied for their endocrine disrupting effects in largemouth bass, there is little information for toxaphene. In this study, male and female largemouth bass were given food containing 50 mg/kg toxaphene for almost 3 months, to achieve tissue levels similar to those found in fish at Lake Apopka. Sex-specific toxicity was then evaluated by measuring various reproductive endpoints and transcriptomic changes. In females, gonadosomatic index showed a trend towards reduction ($p = 0.051$) and plasma vitellogenin was reduced by ~40% relative to controls. However plasma levels of 17β-estradiol and testosterone were not perturbed by toxaphene exposure. These data suggest that toxaphene does not act as a weak estrogen as many other organochlorine pesticides do, but rather appears to be acting as an antiestrogen in female fish. There were no obvious changes in the gonadosomatic index and plasma hormones in male bass. However, ex vivo explant experiments revealed that toxaphene prevented human chorionic gonadotropin-stimulated testosterone production in the testis. This suggested that toxaphene had anti-androgenic effects in males. Subsequent transcriptomic analyses of the testis revealed that androgen receptor/beta-2-microglobulin signaling was up-regulated while insulin-related pathways were suppressed with toxaphene, which could be interpreted as a compensatory response to androgen suppression. In the male liver, the transcriptome analysis revealed an overwhelming suppression in immunerelated signaling cascades (e.g. lectin-like receptor and ITSM-Containing Receptor signaling, CD16/CD14 Proinflammatory Monocyte Activation, and CD38/CD3-JUN/FOS/NF-kB Signaling in T-cell Proliferation). Overall, this study showed that toxaphene induced sex-specific effects. The transcriptomic and physiological responses observed can contribute to the development of adverse outcome pathways for toxaphene exposure in fish.