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Chronic exposure to low environmental concentrations and legal aquaculture doses of antibiotics cause systemic adverse effects in Nile tilapia (*Oreochromis niloticus*) and provoke differential human health risk

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Antibiotics used globally to treat human and animal diseases exist ubiquitously in the environment at low doses because of misuse, overdose and poor absorption after ingestion, coupled with their high-water solubility and degradation resistance. However, the systemic chronic effects of exposure to low environmental concentrations of antibiotics (LECAs) and legal aquaculture doses of antibiotics (LADAs) in fish and their human health risk are currently unknown. We investigated the *in vivo* chronic effects of exposure to LECAs and LADAs using oxytetracycline (OTC) and sulfamethoxazole (SMZ) in Nile tilapia, (*Oreochromis niloticus*) and their human health risk. Twenty *O. niloticus* weighing 27.73±0.81 g were exposed to water containing LECAs (OTC at 420 ng/L and SMZ at 260 ng/L) and diets supplemented with LADAs (OTC 80 mg/kg/day and SMZ 100 mg/kg/day) for twelve weeks. General physiological functions, metabolic activities, intestinal and hepatic health were systemically evaluated. The possible human health risks of the Nile tilapia fillets in adults and children were assessed by using risk quotient. After exposure, we observed retarded growth performance accompanied by reduced nutrients digestibility, feed efficiency, organ indices, and lipid body composition in treated fish. Antibiotics distorted intestinal morphological features subsequently induced microbiota dysbiosis and suppressed intestinal tight junction proteins. Exposure of fish to LECAs and LADAs induced oxidative stress, suppressed innate immunity, stimulated inflammatory and detoxification responses, concomitantly inhibited antioxidant capacity and caused lipid peroxidation in intestine and liver organs. Both LECAs and LADAs enhanced gluconeogenesis, inhibited lipogenesis and fatty acid beta oxidation in intestine and liver organs. The exposure of fish to LECAs and LADAs induced anaerobic glycolytic pathway and affected intestinal fat catabolism in intestine while halted aerobic glycolysis, increased hepatic fat catabolism, and induced DNA damage in liver. The hazard risk quotient in children for fish treated with OTCD was >1 indicating human health risk. Overall, both LECAs and LADAs impair general physiological functions, nutritional metabolism, and compromise fish immune system. Consumption of fish fed with legal OTC provokes health risk in children. Global stringent prohibition policy for use of antibiotics in aquaculture production and strategies to limit their release into the environment are urgently required to protect human health. .

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