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Single microcystin exposure impairs the hypothalamic-pituitary-gonadal axis at different levels in female rats

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ABSTRACT

Microcystin (MC) is most common cyanobacterial toxin. Few studies have evaluated the MC effects on the hypothalamic-pituitary-gonadal (HPG) axis and metabolic function. In this study, we assessed whether MC exposure results in HPG axis and metabolic changes. Female rats were exposed to a single dose of MC at environmentally relevant levels (5, 20 and 40 μg/kg). After 24 h, we evaluated reproductive and metabolic parameters for 15 days. MC reduced the hypothalamic GnRH protein expression, increased the pituitary protein expression of GnRHr and IL-6. MC reduced LH levels and increased FSH levels. MC reduced the primary follicles, increased the corpora lutea, elevated levels of anti-Müllerian hormone (AMH) and progesterone, and decreased estrogen levels. MC increased ovarian VEGFr, LHr, AMH, ED1, IL-6 and Gp91-phox protein expression. MC increased uterine area and reduced endometrial gland number. A blunted estrogen-negative feedback was observed in MC rats after ovariectomy, with no changes in LH levels compared to intact MC rats. Therefore, these data suggest that a MC leads to abnormal HPG axis function in female rats.

1. Introduction

Industrial progress has resulted in the improper disposal of wastewater containing pollutants into rivers and lakes (S. Liu, He, and Li 2022; H. Z. Zhang et al., 2011). Consequently, this process has led to an increase in the incidence of cyanobacteria proliferation, resulting in the production of microcystins (MCs) and harmful algal blooms (HABs) (Du, 2019). HABs have had a detrimental impact on the public health and economy of nearby communities. Currently, approximately 60,000 people suffer from the consequences of HABs every year (S. Liu, He, and Li 2022). Since 2007, the cost of cleaning up Taihu Lake in China has exceeded 16 billion US dollars (H. Zhang et al., 2013). In California, USA, the fishing season was delayed by 6 months as a consequence of HABs, resulting in over $25 million in relief aid being distributed to impacted fishing industries (Free et al. 2022; Holland and Jerry, 2020).

MCs are a group of cyclic heptapeptides in which amino acid residues 2 and 4 vary as L-amino acids. To date, more than 279 MC variants have been reported (Bouaïcha, 2019). Among these variants, MCs that contain leucine (L) at position 2 and arginine (R) at position 4 (MC-LR) are the most extensively studied due to their toxicity and prevalence (Mantzouki et al., 2018). MC-LR in water reservoirs has been reported to have a half-life of approximately one week. In some cases, a lag phase for biodegradation lasting from 9 to 14 days has been reported (Edwards et al., 2008; WHO 2020). However, the half-life of MC-LR in a natural system is estimated at 90–120 days per meter of water depth (Welker and Steinberg 2000). The half-life of MCs is species-specific, ranging from 0.7 to 3.5 days or 2.8–8.4 days in carp (Adamovský, 2007). MC-LR appears to be rapidly absorbed from the gastrointestinal tract into the bloodstream and is quickly transported to the liver, with MC-LR reaching the liver within 1 h after exposure and reaching maximum levels 3 h after exposure. The half-life of MCs in the blood is 3.3 h (Tencalla and Dietrich 1997).

MCs induce a variety of toxic responses in numerous organs, including the liver, kidney, lungs, and reproductive organs (Chen et al., 2016; Gorham et al., 2020; McLellan and Manderville 2017). MCs can enter cells through organic anion transporting polypeptides, leading to

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