

# Effects of the synthetic progestin levonorgestrel on zebrafish (*Danio rerio*) reproduction

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Pharmaceuticals have emerged as a new important class of environmental contaminants. Special concern has been raised about steroidal hormones, which are present in the aquatic environment in many countries in the western world. Most attention has been given to estrogenic steroidal hormones, which are well known to cause endocrine and reproductive disruption in fish at the low concentrations in which they are found in the aquatic environment. Synthetic progestins are used in contraception, and are the compounds chiefly responsible for the contraceptive effect. Progestins are, like estrogens, not efficiently removed by sewage treatment plants (STP:s) and are also widespread contaminants in the aquatic environment. Two previous studies have confirmed the suspicion that progestins cause an inhibition of reproduction in fish similar to their effect in humans, and do so at concentrations found in the environment. In this study, the effects of the synthetic progestin levonorgestrel on the reproduction of zebrafish (*Danio rerio*) were examined. Adult zebrafish were semi-statically exposed to levonorgestrel concentrations of 8.1, 90.4, 158.8 and 654.2 ng L<sup>-1</sup> for 21 days. Levonorgestrel did not cause any statistically significant impairment of reproduction. The results might however indicate that levonorgestrel can cause inhibition of zebrafish fecundity (egg production) similar to that reported in previous studies, although not at environmentally relevant concentrations. In the group exposed to the highest levonorgestrel concentration, there was a trend of decreased gene expression of the reproductive hormones FSH (follicle stimulating hormone) and LH (luteinizing hormone) in the brain. A trend in the opposite direction was observed in the gene expression of GnRH (gonadotropin releasing hormone). These results give an indication that the mechanism behind the previously reported reproductive toxicity of synthetic progestins might occur at the level of neuroendocrine control of reproduction in the brain.

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