ABSTRACT
This project was part of a larger study which was focused on investigating the influ-ence of hepatotoxic substances on the vitellogenin (VTG) production in adult zebrafish (*Danio rerio*). VTG is a precursor of lipoproteins and phosphoproteins that make up most of the proteins found in yolk. VTG is produced in the liver of almost any oviparous animals, mainly females. Its synthesis is induced by estrogenic hor-mones. Accordingly, it has become an important biomarker for the detection of endo-crine-disruptive effects in fish. However, the production of VTG might be modified not only by typical endocrine-associated signalling pathways, but also by non-endocrine-mediated processes. In particular, hepatotoxicity, i.e. the toxicant-induced impairment of liver structure and function, could affect the production of VTG in hepatocytes. For the present study, acetylsalicylic acid (ASA, “aspirin”), a substance well characterized as hepatotoxic in mammals, was used as a model substance. ASA is a non-steroidal anti-inflammatory drug, an antipyretic and an antiplatelet agent. The effect of ASA is based on an irreversible inhibition of cyclooxygenases COX-1 and COX-2.
The hypothesis of the study was that ASA exposure will disrupt normal liver functions in zebrafish and will thus indirectly disrupt VTG synthesis in hepatocytes of exposed fish. This sub-project investigated the effects of ASA on the expression of various endocrine-associated (vtg1, vtg3 and esr1) and hepatotoxicity-related (fabp10a, apoa1, cyp2k19 and cyp3a65) marker genes in female and male zebrafish livers by means of real-time qPCR analyses. Adult zebrafish were exposed to different con-centrations of ASA (0, 10, 50, 75 and 100 mg/L) according to OECD guideline 230 (“21-Day fish assay”).
The exposure induced a decrease in VTG protein levels; this could be inversely cor-related with the pathological effects of karyopyconosis in the zebrafish liver. In male zebrafish liver, apoa1 showed an up-regulation at gene expression level and in fe-male zebrafish, an up-regulation of the hepatotoxicity-related genes (fabp10a, cyp3a65) is seen in contrast to a down-regulation of cyp2k19. With respect to the endocrine-related genes, a significant up-regulation of vtg1 and esr1 in female liver could be detected. Thus, a hepatotoxicity-related and endocrine-related gender-specific effect could be determined in this study.