



Zebrafish Embryo-Larvae: Model of Ototoxicity

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Hearing loss is a worldwide problem influencing quality life of the affected individual. It can occur due to aging (age-related hearing loss), environmental toxins or noise with high frequencies, but most commonly due to exposure to ototoxic drugs. Hair cells, the end organ of the auditory pathway is the affected target organ leading to hearing loss¹². Unfortunately, several drugs used to treat life-threatening illnesses are known to damage hair cells³. These include, aminoglycoside antibiotics, antimicrobials, loop diuretics, anti-inflammatory agents, antimalarial drugs, and platinum-based cytostatic drugs used as chemotherapeutic agents⁴.

Recent research has concentrated on understanding the mechanisms of ototoxic drug-induced inner ear damage and on identifying anti-ototoxic compounds. Since auditory cell-lines cannot alternate with the mature hearing organ, several animal models like rats, guinea pigs, mice and zebrafish (*Danio rerio*) are used in ototoxicity research. Zebrafish and human models share considerable similarities and hence, several human pathological conditions can be screened using zebrafish as a model organism.

The zebrafish larvae inner ear mainly consists of three semi-circular canals and two otoliths (ear stones) attached to two maculae in the otic vesicle. Otoliths, the crystalline structures of calcium carbonate (CaCO_3) contribute to the vestibular function of the animal by transmitting sound vibrations and acceleration forces to the ciliary bundles of macular hair cells⁵. The easy accessibility to the hearing organ, the small size, high fecundity, transparent embryos, low cost in husbandry with less space requirement, and the structural and functional similarities between zebrafish and mammalian hair cells with functional hair cells matured by 3-day post-fertilization (dpf), make zebrafish a valuable animal model for studying hearing loss.

At JRF, we successfully developed ototoxic model of zebrafish embryo-larvae. We used known teratogenic chemical to induce ototoxicity. Zebrafish embryos [24-hour post-fertilization (hpf)] were exposed to sub-lethal concentrations of the ototoxic agent along with appropriate control. At 96 hpf, the larvae were anaesthetized and imaged using bright field microscope focusing the otoliths and otic vesicle. As compared to the development of normal otoliths formed in the control larvae, teratogen treated zebrafish larvae exhibited ototoxicity which was evident by their potential to reduce and deform the otoliths and otic vesicle.



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This zebrafish model of ototoxicity can be employed as a high throughput screening tool to screen compounds with potential ototoxic effect and as a drug discovery tool to screen anti-ototoxic compounds.

Keywords: zebrafish, teratogen, ototoxicity, drug discovery

Note: Kindly contact our business development team for any further details of this model.

References

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Nilambari is a Senior Research Officer in the Ecotoxicology section. She has a good experience of conducting ecotoxicology studies and is actively involved in research validations. She has professional experience of more than 13 years, including academic research, pharmaceutical R&D and CRO industry with several national and international publications.



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