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Zebrafish as a valuable vertebrate model to study teratogenicity of pharmaceuticals and psychoactive substances

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Abstract

Background: The number of pharmaceuticals and psychoactive substances on the market increases each year, posing a need to understand their teratogenic effects on vertebrates. In the last two decades, there has been a growing interest in alternative vertebrate models, as part of the 3 R's principle (Replacement, Reduction, and Refinement) which led to the increased use of the zebrafish (Danio rerio) [1]. Besides, the easy observation of embryo development and the early developmental stages are not classified as experimental animals in the guidelines of the European Directive 2010/63/EU [2], which highlights the ethical advantages in teratogenic potential evaluation [3]. Objective: The study aimed to make a minireview of zebrafish as a model to assess the potential of teratogenicity of pharmaceuticals and psychoactive substances and analyse the major methodologies used to evaluate the malformations severity. Methods: The scientific literature search was done using ScienceDirect and PubMed search engine, looking for: zebrafish, Danio rerio, ecotoxicology, toxicology, malformations, teratogenicity, teratogen potential, and a selection of original papers and review was done. Results: This review confirm that zebrafish is a good model to make a pre-screening of the teratogenicity of pharmaceuticals and psychoactive substances, among others. However, the results reflect that several methodologies are used to assess the zebrafish malformations, showing a high variability and inconsistency in the evaluated endpoints and the nomenclature used. Additionally, each study uses its own scale of malformations severity, which can be evaluated using a quantitative method (different degrees of severity) or a binary method (present or absent). **Conclusions:** Zebrafish are a suitable alternative and complementary model to rodents (and other vertebrates) for massive screening of the potential teratogenic substances despite presenting differences for rodents. In addition, there is a need to standardize the classification and severity system for assessing malformations to improve the reproducibility and comparison between studies.

Keywords: Zebrafish; teratogenicity; psychoactive substances; animal model

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References

- Bauer, B.; Mally, A.; Liedtke, D. Zebrafish embryos and larvae as alternative animal models for toxicity testing. Int. J. Mol. Sci. 2021, 22, 13417.
- Commission, E., Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations
 and administrative provisions of the Member States regarding the protection of animals used for experimental
 and other scientific purposes. OJ L 1986, 358, 1-28.

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3. Raghunath, A., Perumal, E. Analysis of lethality and malformations during zebrafish (Danio rerio) development. In *Teratogenicity Testing. Methods in Molecular Biology*. Félix, L. Eds.; Humana Press, New York, 2018; Volume 1797, pp. 337-363.



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