

# A novel method for the zebrafish depigmentation resulting in an attractive animal model for *in vivo* research



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## DESCRIPTION OF THE INVENTION

The invention refers to a method of depigmentation of zebrafish (lat. *Danio rerio*), within zebrafish animal model, and relies on preparation of a medium for fish, containing an active compound, isoetharine, being a  $\beta$ 2-adrenergic receptor agonist. The obtained model of transparent, embryonic form of zebrafish can facilitate observation of life processes taking place inside the living organism. The technique of obtaining transparent zebrafish using isoetharine is fast and straightforward. The developed animal model represents an inexpensive alternative to the commercially-available transparent casper lines, due to the lack of necessity of carrying out complex genetic crosses.

## EFFECTS OF APPLYING THE INVENTION

Drug discovery is a long and complex process. Currently, many pharmaceutical companies face the challenges of increased costs and reduced efficiency of various steps involved in drug development.

The stages between the discovery of potentially active (ca. 5,000 - 10,000 chemical compounds) and the selection of the most promising molecules (ca. 5 compounds) that will be evaluated in the next phases of clinical trials, usually take 2 to 6 years. In addition, the costs of these stages of research cost up to 300 million USD. The proposed model may contribute to obtaining faster, more efficient, but most of more reliable results obtained during the initial screening tests. Therefore, the associated time and costs of the entire process of designing and testing new drugs and toxicological diagnostics, including ecotoxicology, may be reduced as well.

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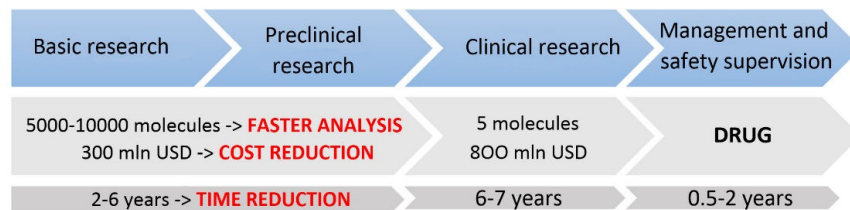
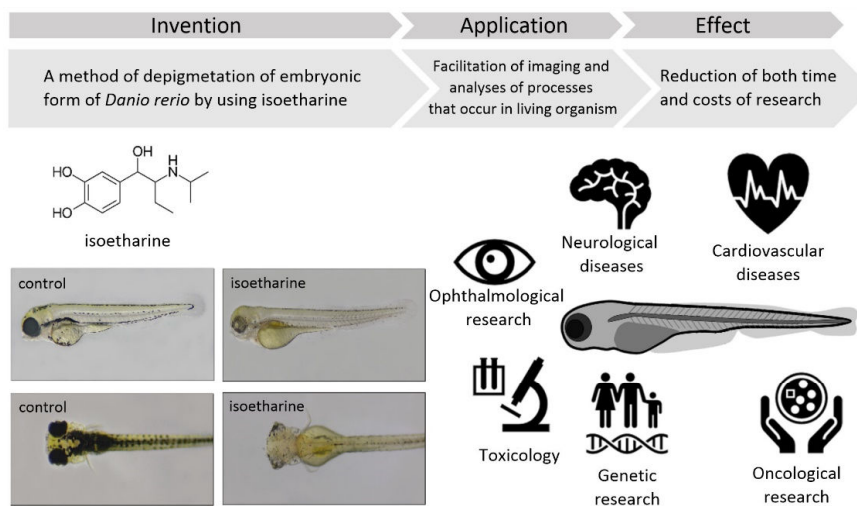
## POTENTIAL APPLICATIONS

The main reasons for the failure of clinical trials are the ineffectiveness of a potential drug candidate against a given disease, as well as the lack of safety of test substances. As much as 17% of rejected drugs are those that cause dangerous side effects, not observed in the earlier stages of preclinical research. In recent years, zebrafish has become an increasingly used model in preclinical research. Therefore, the proposed invention (isoetharin as a compound that induces the transparency of the embryonic form of zebrafish) may play an important role in the first *in vivo* stage of finding new drugs (basic research and preclinical research).

The proposed model combines the following two important innovations: (1) easy and cheap access, allowing for its use in any research laboratory, and (2) facilitating the analysis of *in vivo* processes. More precisely, it enables imaging and analysis of physiological parameters (e.g. heart beat rate, blood flow) and organ development (e.g. pancreas, liver, nervous system, angiogenesis). Interestingly, the proposed model also inhibits the formation of zebrafish eye pigmentation. Due to this effect, the related model can be used during initial ophthalmic examinations, making the proposed model unique in comparison to competitive animal models.

The model can be used in research focused on the organ development and body functions, disease pathogenesis (cardiovascular diseases, neurological diseases, oncology research) and drug testing in order to develop new effective treatments for diseases. Moreover, it can facilitate the assessment of the toxic properties of chemicals contained in pharmaceutical products, plant protection products and industrial chemicals (general toxicology, organ toxicology and ecotoxicology).

The proposed model can be used by both in the research units (universities, research units of the Polish Academy of Sciences, research institutes and international research institutes) and companies, mainly pharmaceutical companies (e.g. Creative Biostructure; Biobide; Roche; ZeClinics).



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Evaluation of  $\beta$ -adrenergic ligands for development of pharmacological heart failure and transparency models in zebrafish

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