

## Drug discovery research for a safe melanin production inhibitor using zebrafish as a vertebrate model

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In Europe, animal testing on cosmetics has been banned without exception since 2013, and globally, animal testing tends to be avoided. The international trend of conducting animal experiments based on the concept of the 3Rs (Reduction, Replacement, Refinement) is becoming more and more established, and when conducting animal experiments, it is required to use animal species with as little or no sensation as possible. Meanwhile, in the process of searching for new cosmetic raw material candidates, it is desirable to discover more effective and safer ones at an early stage.

In this study, we used zebrafish, a well-known vertebrate model organism, to search for new cosmetic materials from natural resources and to verify the usefulness of zebrafish as a method for evaluating new cosmetic material candidates. Zebrafish from the embryonic stage to just after hatching were used to screen for natural resource samples that inhibit melanin pigment production in zebrafish, and a total of five compounds were isolated from two microbial culture extracts. Of these, compounds S2 and F1 effectively inhibited melanin pigment production in zebrafish without any obvious toxicity. For the purpose of comparison, a search study was performed from plant extracts that show tyrosinase inhibitory activity *in vitro* but not melanin pigment inhibitory activity in zebrafish. As a result, 20 compounds were isolated, three of which were new compounds. None of the obtained compounds showed melanin pigment inhibitory activity in zebrafish, and some of them showed hatching inhibitory activity. These results suggest that the search for melanin production inhibitors using zebrafish is a useful approach for early evaluation of the efficacy and potential toxicity of candidate materials for cosmetics to the living body.