Thyroid disruption and associated toxicological outcomes of major organic UV filters in zebrafish

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INTRODUCTION

Organic UV filters are widely used for skin protection in personal care products such as sunscreen, cosmetics, and hair products. Although several UV filter agents such as benzophenone-3 (BP-3) and octyl methoxycinnamate (OMC) have been banned for use in sunscreens in some regions, many organic UV filters are still extensively used for various applications. Most organic UV filters can penetrate skin following dermal application and reach the bloodstream at levels that warrant caution. However, toxicological information is mostly limited to BP-3. Growing laboratory and epidemiologic evidence shows that organic UV filter agents could affect the endocrine system and possibly impair behaviour and the kidneys. In this study, we chose several major organic UV filters and evaluated their potential for endocrine disruption and adverse effects on neurobehaviour and the kidneys.

METHODOLOGY

Six organic UV filters were selected as study chemicals – avobenzone (AVB), BP-3, bemotrizinol (BEMT), diethylamino hydroxybenzoyl hexyl benzoate (DHHB), octocrylene (OC) and OMC. The Hwahea database, which includes ingredient information of sunscreen products being sold on the Korean market (n=2183 as of May 2019), was used to determine the use pattern of the UV filters. Thyroid endocrine disrupting potentials and their related mechanisms were investigated in embryo-larval zebrafish (Danio rerio, <4 hours post fertilisation) following 120 hours of exposure and in adult fish following 21 days of exposure. In addition, the effects on the neurodevelopment and behaviour or kidney toxicity in fish were evaluated.

RESULTS

Among twenty organic UV filter agents used in sunscreens, OMC (59.7 %) and OS (48.8 %) were used most frequently, followed by BEMT (42.2 %). After exposure to several UV filters including AVB, BP-3, DHHB, OC and OMC, thyroid hormone levels and genes related to thyroid hormone regulation were significantly altered in either embryo-larval or adult male zebrafish. In addition, neurobehavioural changes were observed, together with changes to

key genes related to neurodevelopment or neurogenesis. Moreover, AVB, BP-3 and OMC exposure caused proteinuria, transcriptional changes in genes related to kidney structure and injury in embryo-larval zebrafish. AVB, BP-3, DHHB and OMC significantly decreased thyroid hormone levels of embryo-larval or adult male zebrafish and OC significantly increased thyroid hormone levels of embryo-larval zebrafish. In addition, exposure to AVB, BP-3 and OMC significantly induced hypoactivity whereas OC exposure increased the activity of embryo-larval zebrafish when compared to the control group. AVB, BP-3 and OMC also demonstrated increased proteinuria levels in embryo-larval zebrafish. However, no effects were observed for OC.

DISCUSSION

In this study, we found that many organic UV filters disrupt the thyroid hormone balance of both embryo-larval and adult fish, and moreover damage the normal kidney function and neurobehaviour of the fish. In previous studies, thyroid disrupting, neurotoxic and nephrotoxic potentials of BP-3 have been demonstrated in experimental models and humans. It is noteworthy that other frequently used UV filters may cause not only thyroid endocrine disruption but also toxicities affecting behaviour and the kidneys. UV filters are designed to remain on the skin for a long time and can penetrate the dermis to reach the circulation system, which means that their implication in human health is a major public health concern. Moreover, many UV filters are used in combination. Understanding and modelling their mixture toxicity is therefore an urgent task, in order to guarantee the safe use of the sunscreen. The consequences of UV filter exposure during susceptible periods of life, e.g. foetus, infant, and puberty, are in question and warrant rigorous experimental and epidemiological investigations.