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Review:

UV-filter pollution: current concerns and future prospects

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Abstract

UV-filters are widely used in cosmetics and personal care products to protect users' skin from damage caused by ultraviolet (UV) radiation from the sun. Globally, an estimated 16,000 to 25,000 tonnes of products containing UV-filters were used in 2014 with modern consumption likely to be much higher. Beyond this use in cosmetics and personal care products, UV-filters are also widely used to provide UV-stability in industrial products such as paints and plastics. This review discusses the main routes by which UV-filters enter aquatic environments and summarises the conclusions of studies from the past 10 years that have investigated the effects of UV-filters on environmentally relevant species including corals, microalgae, fish and marine mammals. Safety data regarding the potential impact of UV-filters on human health are also discussed. Finally, we explore the challenges surrounding UV-filter removal and research on more environmentally friendly alternatives to current UV-filters.

Key words:

Ecotoxicology, endocrine-disrupting chemical, microplastics, oxybenzone, UV-filter.

Introduction

There is growing concern regarding the role of personal care products (PCPs) in the pollution of aquatic environments (e.g., Ebele, Abou-Elwafa Abdallah and Harrad 2017). This concern has, for example, influenced the use of microplastics (MPs) (Dauvergne 2018), plastic particles smaller than 5 mm in diameter (Lusher *et al.* 2015). MPs are either specifically manufactured for the cosmetic industry for use in products such as facial cleaners and toothpastes (primary MPs), or are produced by the degradation of larger pieces of plastic (secondary MPs) (Kalčíková *et al.*

2017). MPs have been found in many aquatic environments, and in the tissues of invertebrates, fish, and large aquatic mammals including whales and seals (Karlsson *et al.* 2017; Zhu *et al.* 2019; Donohue *et al.* 2019; Hernandez-Milian *et al.* 2019; Moore *et al.* 2020; Burkhardt-Holm and N'Guyen 2019). The prevalence of MPs, combined with their potentially toxic effects, has led to the re-evaluation of their use in cosmetics (Lam *et al.* 2018). For example, in 2018 concerns regarding PCPs resulted in the United Kingdom banning the use of primary MPs in any consumer products as part of their 25 Year Environment Plan (Kentin and Kaarto 2018). Other countries, including the United States, Canada and Australia, have now also limited or banned the use of primary MPs (Lam *et al.* 2018).

Another commonly used component of many cosmetics and PCPs are ultraviolet (UV) light filters (UV-filters) (Osterwalder, Sohn and Herzog 2014). UV-filters are commonly used as UV-stabilizers for products such as perfumes, or as UV-protection in products such as moisturisers, tanning and sun-protection products (Blüthgen, Zucchi and Fent 2012). UV-filters are also used worldwide in a large range of industrial products (Molins-Delgado *et al.* 2017). In these industrial situations they are used as additives to reduce the degradation rate of plastics and paints when they are exposed to the sun's ultra-violet rays (Fent, Zenker and Rapp 2010; Wojciechowski *et al.* 2015).

Generally, UV-filters can be categorized into two groups: organic and inorganic (Morlando *et al.* 2016). Organic UV-filters are chemicals that absorb the sun's UVA and/or UVB rays (Serpone, Dondi and Albini 2007), with the most commonly used organic UV-filters being oxybenzone (BP-3), octinoxate (ethylhexyl methoxycinnamate or EHMC), 4-methylbenzylidene camphor (4-MBC), octyl dimethyl p-aminobenzoate (OD-PABA), and octocrylene (OC) (Tsui *et al.* 2014).

Titanium dioxide (TiO_2) and zinc dioxide (ZnO) are the most common inorganic UV-filters (Morlando *et al.* 2016), with these functioning due to their ability to reflect or refract UVA and/or UVB (Serpone, Dondi and Albini 2007).

In 2014 it was estimated that between 16,000 and 25,000 tonnes of products containing either organic or inorganic UV-filters were being used worldwide (Díaz-Cruz and Barceló 2009; Osterwalder, Sohn and Herzog 2014; Wu *et al.* 2016). Although more recent global estimates are not available, usage of products containing UV-filters in the U.S. alone is now estimated to be between 9,000 and 32,000 tonnes annually (Narla and Lim 2020). This substantial growth is likely due to an increased public awareness of environmentally influenced conditions such as skin cancer and premature skin aging and the increased recommendations by dermatologists (Osterwalder, Sohn and Herzog 2014; Leiter, Keim and Garbe 2020).

Similar to the case of MPs, there are now growing concerns regarding the potential of UV-filters to act as pollutants (Schneider and Lim 2019a). However, in contrast to MPs, UV-filters are still widely available to consumers around the world. With this in mind, here we review the various types of UV-filters, their prevalence worldwide, and their eco-toxicological potential. Finally, we consider the improvements that could be made in the management of these pollutants and reflect on some future research priorities.

Organic UV-filters

The chemical properties of organic UV-filters make them especially suitable for their role as topical skin barriers. For example, many organic UV-filters are large molecules with aromatic moieties comprised of carbonyl-groups or methoxy-groups (Hopkins, Snowberger and Blaney

2017), and their molecular structure gives them a high UV-filtering potential over a range of UV wavelengths (280 nm to 400 nm) (Hopkins and Blaney 2016). It is also thought that these large aromatic moieties generally result in low levels of skin permeability (Zhang *et al.* 2017). For example, Hewitt *et al.* (2020) found that benzophenone had a skin permeability of 0.87 $\mu g.cm^{-2}$ after 24 hours, which is more than 10-fold lower than that of many other cosmetic components such as the fragrance Anisyl alcohol (skin permeability of 10.15 $\mu g.cm^{-2}$ after 24 hours). Despite this, some studies have suggested that, despite the low skin permeability, between 1-10% of benzophone-3 (BP-3) is absorbed through the skin and excreted in urine (Gonzalez *et al.* 2006; Cozzi, Perugini and Gourion-Arsiquaud 2018; Souza and Maia Campos 2017). That said, the skin permeability of BP-3 and other UV-filters may be even higher than that detected in urine due to accumulation within cells resulting from their lipophilic properties and low water solubility (represented by a high Log-k_{ow} value, the octanol-water partition value that is used to assess the bio-accumulation factor of a chemical) (Gago-Ferrero, Díaz-Cruz and Barceló 2011; Badia-Fabregat *et al.* 2012; Nakata, Murata and Shinohara 2009). Specifically for BP-3, this type of bio-accumulation has been demonstrated, with a far higher concentration of BP-3 found in human adipose tissue (>5 $\mu g.L^{-1}$) than that detected in urine samples (>0.4 $\mu g.L^{-1}$)(Wang, Asimakopoulos and Kannan 2015).

Although it is uncertain exactly how much gets absorbed by the skin, the majority of UV-filters will, either directly or indirectly, enter our marine or freshwater environments through activities such as swimming or via showering and urination (Gonzalez *et al.* 2006). This has been evidenced by the sampling of surface water from large metropolitan areas (containing both commercial and industrial developments) around the world that found that UV-filter concentrations increased in line with population density and was higher in areas with poor waste-water-treatment (WWT) strategies (Tsui *et al.* 2014). In combination, this suggests that a large proportion of the UV-filter pollution comes from the plumbing system. Further evidence for the entry of UV-filters into marine environments was provided by sampling of both surface water and column water from areas in France used for recreational swimming, with this showing higher concentrations of UV-filters in recreational areas than off-shore, and fluctuations in the concentration that tracked the number of beach-goers (Labille *et al.* 2020). Similarly, a seasonal increase of 27% in the total UV-filter concentration was detected in rivers and waste-water-treatment (WWT) plant effluents during the summer months (Ekpeghere *et al.* 2016).

Ineffective WWT methods themselves also play a considerable role in organic UV-filter pollution (Ekpeghere *et al.* 2016; Tsui *et al.* 2014). One commonly used WWT strategy is the use of activated sludge, where flocs of bacteria, protozoa, and other microorganisms are used to breakdown organic UV-filters. However, due to their high log-k_{ow} values, organic UV-filters tend to accumulate within the sludge making biodegradation ineffective (Badia-Fabregat *et al.* 2012). An example of this was seen in a study that investigated the effectiveness of activated sludge treatment, where it was found that only 28-51% of BP-3 was removed from the water (Vassalle *et al.* 2020). Physical WWT strategies such as UV-radiation treatment have also been shown to be ineffective in removing UV-filters; for example, Gago-Ferrero *et al.* (2012) found that both BP-3 and BP-1 were poorly degraded by UV exposure, with no decrease in BP-3 level observed after 24 hours of treatment.

Inorganic UV-filters

In contrast to the situation with organic UV-filters, it is believed that inorganic UV-filters have negligible skin permeability due to their large particle size and insoluble nature (Kim *et al.* 2017; Tang *et al.* 2018). Given their low skin absorption potential, it can be assumed that inorganic UV-filters also get washed off and enter water supplies in a similar manner to organic UV-filters (Gondikas *et al.* 2014). Unlike organic UV-filters however, inorganic UV-filters are more effectively removed in WWT plants; in fact it has been calculated that modern day WWT plants remove up to 90% of TiO_2 from influents (Mahlalela, Ngila and Dlamini 2017). Despite this, TiO_2 has been detected in post-treatment effluents of WWT plants around the world at measurable levels (between 0.5 and- 6.5 $\mu g.L^{-1}$ (Neal *et al.* 2011; Gondikas *et al.* 2014). The fact that TiO_2 is still detectable post- treatment has raised concern for the levels of TiO_2 in untreated waters as this could lead to pollution caused by WWT overflow spills. Wang *et al.* (2020) estimated that the levels of TiO_2 could reach as high 150 $\mu g.L^{-1}$ in untreated wastewater. Furthermore, TiO_2 has been shown to accumulate within the biosolids of sewage sludge as well as potentially in sediments polluted by untreated waters. Gottschalk *et al.* (2015) estimated that the amounts of TiO_2 in such areas could exceed 100 $mg.kg^{-1}$. The fact that sewage sludge from WWT plants is sometimes used as fertiliser also amplifies the risk that sediment-dwelling and soil-dwelling organisms could be exposed to high amounts of TiO_2. Given that TiO_2 is considered moderately toxic by the American Environmental Protection Agency (EPA) and has an EC_{50} concentration (the concentration of a chemical at which a 50% reduction in tested endpoints is induced) of between 1 and 10 $mg.L^{-1}$ (Hu *et al.* 2020; Soler de la Vega *et al.* 2021; Gottschalk *et al.* 2015), this exposure could negatively affect such organisms.

UV-filter migration

Organic and inorganic UV-filters have been detected near WWT effluents, nearshore waters, and in recreational sites worldwide (Cadena-Aizaga *et al.* 2020). This is not surprising given how they are used and how they move into both marine and freshwater environments. Unexpectedly, organic UV-filters do not however seem to be limited to these areas. For example, analysis of water from the rural Antarctic peninsula region identified varying levels of organic UV-filters in all samples (Domínguez-Morueco *et al.* 2021). Although some of this UV-filter pollution could be attributed to a small amount of wastewater runoff from the science stations, these data suggest that UV-filters from other, more inhabited, are traveling large distances.

The full extent of UV-filter migration remains unknown, but one possibility is that UV-filter migration is facilitated by MPs (O'Donovan *et al.* 2020). This is possible given that many plastic products already contain UV-filters as preservatives. Moreover, other plastics, such as the low-density polyethylene (LDPE) micro pellets used worldwide in the production of household items, reusable bags and food packaging, have been shown to absorb environmental BP-3 and later release it when consumed by an organism (Kyaw *et al.* 2012; Wu *et al.* 2016). O'Donovan et al. (2020) studied the effects of this on the marine clam, *Scrobicularia plana* and found that MPs containing BP-3 caused oxidative stress in the digestive system, an effect not seen in clams consuming virgin MPs. This study, and other similar work (e.g., Rainieri et al. 2018), argues that the toxic effects of MPs and chemical pollutants can be synergistic. Two hypotheses for this increase in toxicity are that (1) the amount of chemical pollutants released from MPs is higher compared to environmental pollution levels due to accumulation within the MPs (Bakir, Rowland and Thompson 2014), or that (2), contaminated MPs remain in the organism for extended periods of time, therefore increasing the chemical pollutant exposure time (Rainieri *et al.* 2018).

The distribution of MPs has been widely researched (Khatmullina and Isachenko 2017; Iwasaki *et al.* 2017; Courtene-Jones *et al.* 2017); small plastic fragments for example, like those that can absorb UV-filters, have been shown float in the upper water column (<5 m) for extended period of time depending on the type and condition of the plastic (Khatmullina and Isachenko 2017). Floating MPs are subjected to strong surface currents and surface winds, resulting in a large horizontal migration (Reisser *et al.* 2015), this is evidenced by sampling studies reporting large-scale seasonal MP migration coinciding with periods of strong surface currents and surface winds (Iwasaki *et al.* 2017). Eventually MPs travel vertically through the water and settle within the deep sea sediment (Kowalski, Reichardt and Waniek 2016; Courtene-Jones *et al.* 2017). The nature of MPs horizontal and vertical travel within the water column, combined with their ability to absorb and release UV-filters could provide a reasoning for the unexpected travel of UV-filters to remote areas such as the Antarctic region.

Environmental breakdown

It is generally believed that environmental forces contribute heavily to the degradation of chemical pollutants (Ahmed *et al.* 2017), however, this may not be the case for some UV-filters (Rodil *et al.* 2009; Badia-Fabregat *et al.* 2012). For example, EHMC and OP-PADA are both heavily affected by UV-radiation, having half-lives of between 20 and 57 hours (Rodil *et al.* 2009; Badia-Fabregat *et al.* 2012), but BP-3 has shown only a 8% degradation after being exposed to artificial solar light for 20 days (Liu *et al.* 2011). Natural rivers and oceanic sediment also usually play large parts in the bio-degradation of pollutants, however, due to the high Log-k_{ow} value, this process can be limited in the case of some UV-filters (Gago-Ferrero *et al.* 2012). Regardless of the method, the degradation of UV-filters can lead to the release of derivative chemicals due to hydrolysis (Vione *et al.* 2015); indeed, this is the case with EHMC UV-degradation, where the main derivative is 4-methoxybenzaldehyde (Vione *et al.* 2015).

Little is known regarding the environmental fate of inorganic UV-filters, largely due to the lack of qualitative data (Bundschuh *et al.* 2018). This is largely due to the fact that engineered nano-particles, such as those used as inorganic UV-filters, are often undistinguishable from naturally occurring ones and to the fact that environmental concentrations of these particles tend to be relatively low (Bundschuh *et al.* 2018; Schneider and Lim 2019a). Despite this, studies based on batch systems using model compounds and environmental forces suggest that inorganic UV-filters are heavily broken down in the environment due to factors such as water salinity, environmental pH and ionic forces (Bundschuh *et al.* 2018; Schaumann *et al.* 2015; Wong *et al.* 2010; Minetto *et al.* 2017). It is also believed that the environmental degradation of TiO_2 and ZnO nano-particles would lead to the release of Zn+ and $OH^{\cdot}$ free radicals, of which the effects on organisms remains largely unknown (Minetto *et al.* 2017; Haynes *et al.* 2017; Schneider and Lim 2019a).

Effects on the environment

Whilst it is clear that UV-filters are present in our environment at varying concentrations (Tsui *et al.* 2014), their biotic effects remain uncertain. Looking at the effect that UV-filters have on some key ecological species does however give insight into their ecotoxic potential. For example, it is estimated that 40% of coastal coral colonies worldwide are exposed to UV-filter pollution (Downs *et al.* 2016), with exposure to UV-filters linked to coral bleaching (Downs *et al.* 2014;

Corinaldesi *et al.* 2018). Studies have shown that when under the influence of UV-light, BP-3 causes oxidative stress to the thylakoid membrane in zooxanthellae (Downs *et al.* 2016), the dinoflagellates that live in symbiosis with corals, jellyfish and sea sponges, providing them with essential photosynthesis products (Ben-Zvi, Eyal and Loya 2015). The decrease of zooxanthellae within the coral matrix causes the lightening of the brown colour of the corals, a process often associated with the coral bleaching process (Downs *et al.* 2014; Corinaldesi *et al.* 2018). The oxidative stress caused by organic UV-filters when exposed to UV-light is believed to be due to the release of degradation products (Lai, Chen and Lin 2020; Rodil *et al.* 2009). Inorganic UV-filters can also cause damage in this manner, with, for example, the reactive oxygen species produced by the degradation of TiO_2 causing both damage to tissues and to DNA (Zhao *et al.* 2019; Zhang and Sun 2004; Haynes *et al.* 2017; Faria *et al.* 2014).

Microalgae are also a significant part of many aquatic food webs, and are often essential in maintaining ecosystem health (Nava and Leoni 2021). For this reason, studies have started focusing on how UV-filters affect some key algal species. Similar to the damage seen in corals, UV-filters can cause damage to photosynthetic pigment production in algae (Mao *et al.* 2017; Paredes *et al.* 2014). In a study conducted by Mao *et al.* (2017), several model microalgae species were used, including the microalgae *Chlamydomonas reinhardtii,* as bioassays to assess the ecotoxic potential of BP-3. It was concluded that at environmentally relevant concentrations (*i.e.*, 0.1 and 1 $\mu g.L^{-1}$) BP-3 was systematically absorbed by the algae and caused a decrease in chlorophyll *a* (chl-a) (Mao *et al.* 2017). At higher concentrations (>10 $\mu g.L^{-1}$) the decrease in chlorophyll-a, chlorophyll *b* and carotenoid content resulted in a reduction in photosynthetic pigment production which subsequently led to a decrease in growth rate (Mao *et al.* 2017). Another study reported similar results for the micro-algae *Isochrysis galbana* with an EC_{50} of 13.87 $\mu g.L^{-1}$ (Paredes *et al.* 2014).

As well as affecting the pillars of the aquatic ecosystems such as corals and algae, UV-filters have also been shown to directly affect fish (Zhang *et al.* 2016; Tapper *et al.* 2019; Alamer and Darbre 2018). For example, exposure to OCT has been shown to cause an increased vitellogenin (VTG) induction in the model fish species *Danio rerio*, while exposure to BP-3 has been shown to cause an increased VTG induction in rainbow trout (Tapper *et al.* 2019; Zhang *et al.* 2016). VTG is an egg-yolk precursor protein expressed in oviparous female fish as a response to oestrogen signalling within liver cells (Nagler *et al.* 2010). VTG expression in male fish is used as a classic biomarker for endocrine disrupting compounds (EDCs) as it only appears with external oestrogenic exposure (Yamamoto *et al.* 2017; Nagler *et al.* 2010). The presence of EDCs has been shown to be detrimental for both female and male fish fertility; a study in 2008 found that it caused endocrine imbalance, malformation of the gonads, altered social behaviours and a reduced spermatozoa count in males (Xu *et al.* 2008). Interestingly, work focussing on low level EDC exposure in flathead minnows found feminization of male fish and the near extinction of the population within the enclosed testing lake (Kidd *et al.* 2007). Further to this, prenatal 4MCB exposure has also been shown to cause spinal malformation and motility issues in *D. rerio*, with effects observed at exposure concentrations of 3.69 $mg.L^{-1}$ and above (Li *et al.* 2016). Although these levels of 4MCB are approximately 50 times higher than those that are routinely sampled in influents, the high log-K_{ow} value of 4MCB means that it could bio-accumulate within the fish (Balmer *et al.* 2005; Li *et al.* 2016).

UV-filters have also been detected in marine mammals (e.g., Gago-Ferrero *et al.* 2013) and, despite the scarcity of such studies, the maternal transfer of UV-filters has also been demonstrated in two dolphin species, *Pontoporia blainvillei* and *Sotalia guianensis* (Alonso *et al.* 2015). This work found EHMC in both placental and milk samples and in the case of the *P. blainvillei*, EHMC levels in foetal muscle tissue were found to be significantly higher than in the maternal tissue, suggesting efficient maternal transfer of the UV-filter (Alonso *et al.* 2015; da Silva *et al.* 2021).

It has been proven difficult to accurately predict which UV-filters pose a significant environmental threat. It has previously been suggested that environmental risk assessment is dependent on how long the pollutant remain within the environment. For example, EHMC is highly toxic to algae (EC50= 74.72 μg.L-1), but due to its rapid breakdown in the environment it has been deemed to be a low environmental risk (Paredes *et al.* 2014). The hypothesis that environmentally unstable chemicals pose little threat to organisms regardless of toxicity due to limited exposure time, does not however concur with studies such as that of Alonso *et al* (2015) where dolphins were found to have still accumulated these chemicals within their tissues. This highlights the need for more research in this area to better understand the bio-accumulation effect of UV-filters, and to be able to make more accurate environmental risk assessments.

Research in this area is however in its infancy; not only is the exact extent and mechanism of toxicity unknown for many UV-filters, the long-term effects on ecosystems at environmentally relevant concentrations are unknown. Despite this general pattern, BP-3 has been consistently highlighted as a particular concern because it remains stable within the environment, is toxic at relatively low levels, and due to its lipophilic tendency, it also has the ability to accumulate within aquatic organisms (Paredes *et al.* 2014).

Effects on humans

Systematic disruption of neural function

As discussed above, between 1 and 10% of organic UV-filters are believed to penetrate human skin. This, in combination with other exposure routes such as contact with polluted waters, has led to many studies focusing on the potential adverse effects that BP-3 may have on the human body (Cozzi, Perugini and Gourion-Arsiquaud 2018; Souza and Maia Campos 2017). The fact that BP-3 has been detected at very high frequencies in urine (between 94% and 98% of samples taken in America and Denmark respectively), and that it has been found in human breast milk, suggests that most people are, or have been, exposed to BP-3 (Molins-Delgado *et al.* 2018; Calafat *et al.* 2008).

Worryingly, BP-3 has been shown to travel through the blood-brain barrier and can accumulate in the white matter of the brain, with concentrations of up to 0.32 $ng.g^{-1}$ having been found in frozen human post-mortem samples (Van Der Meer *et al.* 2017; Wang, Asimakopoulos and Kannan 2015). Although, in humans, the effects of this are unknown, BP-3 has been shown to induce oxidative stress and apoptosis within the hippocampus and frontal cortex of rat models (Pomierny *et al.* 2019). Furthermore, BP-3 also increased the concentration of extracellular glutamine in the brain of mice (Pomierny *et al.* 2019), a change associated with hippocampal atrophy and diseases such as medication-resistant temporal lobe epilepsy, and in Alzheimer's, Parkinson's and Huntington's disease in humans (Cavus *et al.* 2008).

Oestrogenic disruption

Many studies have suggested that organic UV-filters cause disruption to the endocrine system and could potentially be classified as EDCs (Alamer and Darbre 2018; Wnuk *et al.* 2018; Krause *et al.* 2018; Huang *et al.* 2020). For example, assays using both human cancer cell lines and immature rats have demonstrated oestrogenic effects of the UV-filters 3-benzylidene camphor (3-BC) and 4-MBC (Schlumpf *et al.* 2004; Alamer and Darbre 2018). Here, uterine bioassays in immature rats showed a significant increase in uterine weight (Schlumpf *et al.* 2004). Similarly, the cancer cell work indicated that at concentrations similar to that sampled in human breast milk (Schlumpf *et al.* 2010), EHMC, 4-MBC, BP-3, and homosalate all caused an increase in invasiveness and cell migration of MCF-7 (Alamer and Darbre 2018), a breast cancer cell line with oestrogen, progesterone and glucocorticoid receptors.

Prenatal exposure

It has been shown that BP-3 can penetrate the placental cellular barrier and has been sampled in amniotic fluid, placental tissue and foetal blood, raising potential concerns about its impact on foetal health and development (Vela-Soria *et al.* 2011; Philippat *et al.* 2012; Krause *et al.* 2018; Wnuk *et al.* 2018; Tang *et al.* 2013; Song *et al.* 2020). A study conducted by Wnuk *et al.* (2018) for example, demonstrated that prenatal BP-3 exposure changes the expression of ESR1-ESR2 receptors (ESRs) and G-protein-coupled receptors (GPER1). ESR1 and ESR2 are the major oestrogen receptors responsible for many endocrine processes, but they also play an important role in the maintenance of neural health by inhibiting CASPASE-mediated neural cell death and by maintaining a neutral BCL2-BAX protein ratio (Wnuk *et al.* 2018; Wnuk and Kajta 2017; Zhou *et al.* 2018; Gingerich *et al.* 2010; Foot, Henshall and Kumar 2017). GPER1 receptor signalling is also important in the maintenance of healthy brain function as it plays a major role in the regulation of intra- and intercellular communication and has been shown to provide neural protection by mediating 17β-oestradiol in hippocampal and cortical cells (Lu *et al.* 2016; Wnuk and Kajta 2017; Liu, Lou and Fu 2016). Disruption of either ESRs or of GRER1 signalling could lead to increased levels of neural apoptosis, which has been shown to have severe adverse effects on human development, resulting in anatomic abnormalities and potential mental disabilities (Roth and D'Sa 2001).

Another worrying effect caused by BP-3 was demonstrated by Wnuk *et al*. (2018), who reported that BP-3 inhibited global DNA methylation and decreased DNMT activity. An interruption in DNA methylation caused by an endocrine disruptor, such as BP-3, could induce a multigenerational epigenetic effect by impacting the germ line during the methylation process in a developing gonad (Anway and Skinner 2006; Wnuk *et al.* 2018). It has also been demonstrated that BP-3 can alter the germ line development in rat models; this proved to be detrimental to the rats' fertility, as the early follicle population and the number of mature oocytes was decreased (Santamaría *et al.* 2019).

Prenatal BP-3 exposure has also been shown to induce abnormal migration of the enteric neural crest cells 293T and SH-SY5Y cell lines (Huo *et al.* 2016; Justus *et al.* 2014). Incomplete migration of these cell lines has been shown to result in an absence of ganglia in the distal colon which can lead to the development of Hirschsprung's disease (Szylberg and Marszalek 2014; Meinds *et al.* 2019). This condition causes severe constipation and discomfort in humans and usually results in surgical intervention with many patients continuing to suffer throughout their lives (Meinds *et al.* 2019).

Finally, many studies have suggested that BP-3 affects the growth of human foetuses, although interestingly, here results are conflicting. Whilst some studies have reported an increase in the total foetal growth in both females and males (Philippat *et al.* 2012; Ferguson *et al.* 2018), others have reported a decrease in abdominal circumference in males (Ferguson *et al.* 2018), and the total foetal weight in females (Wolff *et al.* 2008), suggesting more research in this area is needed to clarify the situation.

Effects on puberty

Multiple UV-filters have also recently been linked to changes in the timing of puberty (Huang *et al.* 2020). In this study, almost 300 individuals were assessed using both the Tanner staging method, the medical standard for assessing puberty growth rates (Koopman-Verhoeff *et al.* 2020), and questionnaires in two separate years (2011 and in 2013). The participants also had urine samples taken at both sampling times to assess the prevalence and concentrations of 12 commonly used UV-filters. BP-3 was the most common UV-filter detected, and levels were found to be associated with reduced testicular growth rate, suggesting an anti-androgenic effect on males. Levels of EHMC, another commonly detected organic UV-filter, were also found to be associated with delayed male puberty, while OD-PABA was shown to accelerate female puberty (Huang *et al.* 2020). Whilst this is the first study to look at the epidemiologic effects that UV-filters had on human pubertal development, these results suggest that better understanding the true extent of these effects is a priority.

Current progress and future prospects

Alternatives

Considering the increasing demand for UV-protection products and our current understanding of UV-filter toxicity, many manufacturers and researchers have spent the last decade trying to develop alternative, safer and more environmentally friendly options. For example, BP-3 derivatives have been investigated as potential options, with BP-4 shown to be less toxic then BP-3 having a EC50 value near 10.000 µg.L-1 (slightly toxic) in the algae *Isochrysis galbana*, the crustacean *Scorpaenopsella armata*, the sea-urchin *Paracentrotus lividus* and the bivalve *Mytilus galloprovincialis* (Paredes *et al.* 2014). Although it is believed that the additional sulfonic acid group in BP-4 plays a crucial role in this decreased observed toxicity, further toxicity data are needed to accurately assess its toxicity and suitability as a safe UV-filter (Du *et al.* 2017). Interestingly, toxicity tests such as these ruled out using BP-2, a derivative of BP-3. Originally suggested as a potentially environmentally friendly option, it was since been found that BP-2 is an even more potent EDC due to an increased ability to bind to oestrogenic receptors (Thia, Chou and Chen 2020).

Another possible approach is to develop novel synthetic UV-filters. Avobenzone (AVO) is one such option, with the FDA recently demonstrating a far lower skin absorption capability for AVO than for OXY, with the overall maximum plasma concentrations being 7.1 ng/mL and 258.1 ng/mL respectively (Matta *et al.* 2020; Zhong *et al.* 2020). Although a lower absorption capability is favourable as this reduces the amount of direct exposure to the user via the dermis, the absorption capability of both these chemicals were far above the FDAs threshold of 0.5 ng/mL, prompting the FDA to suggest further investigation. Given that these AVO levels resulted from a single application on 75% of the body, and that beachgoers using suntan lotion report reapplying an average of 2.6 times a day (Labille *et al.* 2020; Ahn *et al.* 2019), levels would be expected to be much higher in real world use.

Aside from the development of more classic UV-filters, as mentioned above, a promising approach to sustainable UV-filter development is to focus on using natural compounds derived from plants and algae. Several studies have identified such extracts showing promising UV-protecting capabilities as well as ROS reducing capabilities. A study by Almeida *et al.,* in 2015 for example found that *Castanea sativa* leaf extract at a concentration of 1 μg/mL was able to reduce the amount of UV-mediated DNA damage in a human keratinocyte cell line by 66.4%. However, despite these discoveries, there are currently no approved sun protection products containing plant extracts as active ingredients. This stems from a number of issues with currently known active ingredients. Firstly, as with organic UV-filters, some natural compounds can potentially have adverse effects on the user. For example, treatment with an extract of edible red seaweed *Eucheuma cottonii* was found to have an antioxidant effect on a human keratinocyte cell line, but caused cytotoxic effects at high concentrations (Lim *et al.* 2015). Secondly, the addition of natural compounds can also alter the stability of a formulation; for example the green *Coffea arabica* seed oil has been shown to have UV-protective capabilities however formulations containing this extract were highly viscosity, making the application of such a product difficult, likely resulting in an insufficient coating of the skin (Wagemaker *et al.* 2015).

WWT improvements

The removal of UV-filters through WWT plants has been shown to be flawed as traditional removal methods are not designed to remove emerging pollutants, resulting in a large amount of UV-filter remaining within the water supply (Tsui *et al.* 2014; Ekpeghere *et al.* 2016; Salthammer 2020). Improvements in the effectiveness of WWT methods could greatly reduce the amount of UV-filter pollution, resulting in a reduction of the environmental risk associated with UV-filter production and use (Vasilachi *et al.* 2021).

Currently, one of the main WWT methods is the use of active sludge. This method relies on flocs of microorganisms suspended freely within a wastewater system to breakdown organic chemicals (Sehar and Naz 2016). However, due to their large structure, lipophilic nature and high bio-accumulation factor, UV-filters are inefficiently broken down and accumulate within the bacterial sludge which then settles to the bottom of the system (Badia-Fabregat *et al.* 2012; Vasilachi *et al.* 2021; Sehar and Naz 2016). The bacterial sludge is then treated as waste and disposed of, potentially resulting in substantial pollution itself (Ji *et al.* 2020).

One suggested way to improve the efficiency of WWT plants is by the incorporation of specific micro-organisms that can metabolize UV-filters. Some novel studies have used the "reverse discovery" method to identify microorganisms that can break down these complex molecules (Suleiman *et al.* 2019). Here, biosolids that showed bio-degradation potential were identified and sampled, and individual microorganism strains within samples were identified and tested for efficiency (Suleiman *et al.* 2019). The fungus *Tinae versicolor* was found to efficiently break down 4-MBC (100% in 24 hours) (Badia-Fabregat *et al.* 2012), and recently, Fagervold *et al.* (2021) found that the bacteria *Sphingomonas wittichii* (stain BP14P) efficiently broke down BP-3 (>95% degradation after 4 days) by using it as a carbon source. The biodegradation of other

UV-filters has however been shown to be more difficult. Fagervold *et al.* (2021) found that with the addition of R2B media, *S. wittichii* also broke down 2-ethylhexyl salicylate (ES) and homosalate, but at low rates (28% and 18% within 14 days respectively). Suleiman *et al.,* (2019) also identified a bacterial species (*Mycobacterium agri)* that broke down 19% of OC within 10 days. Recently a study identified river sediment from China containing an unknown mix of microorganisms were shown to be able to reduce EHMC levels within seven days (Zhang *et al.* 2021).

The use of these effective bacterial and fungal strains could be implemented in WWT plants and tailored to the specific UV-filters that are commonly detected in the influents of that area, resulting in a great improvement in effectiveness of these WWT plants. This, alongside modern treatment strategies such as the implementation of bio-films, membrane filters and constructed wetlands within treatment systems, could provide a much higher degree of UV-filter removal and could partly mitigate the environmental risk some UV-filters pose (Khan *et al.* 2020; Sehar and Naz 2016; Chen *et al.* 2016; Vasilachi *et al.* 2021).

Regulations

Public interest on the effect of UV-filters on corals has led to some countries implementing regulations on the use and distribution of UV-filters. For example, in 2017 the EU reduced the maximum concentration of OXY allowed in PCPs from 10% to 6% (Commission regulation, 2017) . More significantly, in January 2020, the republic of Palau was the first country to ban the use of BP-3, EHMC, octocrylene and 4MBC in PCPs (Republic of Palau, 2018). The island of Aruba quickly followed suit and banned the use, distribution and import of BP-3 in July 2020 (Gobierno Aruba, 2020). Since then, a number of similar bills banning UV-filter use in PCPs have been passed in Hawaii, Bonaire and in some areas of Mexico (Narla and Lim 2020). Although these bans protect areas from direct exposure to UV-filters, ocean currents play a role in the distribution of UV-filters, potentially undermining the effect of local rules. In the case of MPs for example, despite being protected, the Galapagos islands still experience high levels of MP pollution with the great majority believed to be brought in by currents from South America (Jones *et al.* 2021). To combat this effect, both local bans and global regulations would be necessary. Additionally, more studies, such as those performed to investigate MP pollution migration, could provide further insight as to where regulation of the use of UV-filters would best be implemented.

Conclusion

There is evidence to suggest that UV-filters pose an environmental risk due to their various exposure routes, their global prevalence, their high bio-accumulation potential and their known toxicity to environmentally crucial species. It has also been shown that some UV-filters may pose a direct threat to human health due to their ability to migrate through cellular barriers and cause endocrine disruption affecting both early embryonic, and pubertal, development. Beyond this, preliminary studies suggest that some UV-filters could also contribute to the development of degenerative neural diseases.

Although traditional WWT strategies are not designed to handle the pollution from PCPs, changes to the systems currently used may reduce the amount of circulating within our water supply. Such changes in combination with further regulations on the use and distribution of these products and the potential replacement of these with novel environmentally friendly UV-filters could together greatly reduce the amount of harmful UV-filters in our water supply, and the amount reaching our marine and freshwater ecosystems. To achieve this goal however, more research must be performed to further understand the distribution and movement of UV-filters within the environment, and to accurately assess the toxicity of novel UV-filters.

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Reference list

Ahmed, M.B., Johir, M.A.H., Zhou, J.L., Ngo, H.H., Guo, W., Sornalingam, K., (2017). Photolytic and photocatalytic degradation of organic UV filters in contaminated water. *Current Opinion in Green and Sustainable Chemistry*, 6, 85-92. https://doi.org/10.1016/j.cogsc.2017.06.010

Ahn, S., An, S., Lee, M., Lee, E., Pyo, J.J., Kim, J.H., Ki, M.W., Jin, S.H., Ha, J., Noh, M., (2019). A long-wave UVA filter avobenzone induces obesogenic phenotypes in normal human epidermal keratinocytes and mesenchymal stem cells. *Archives of Toxicology*, 93. 1903-1915. https://doi.org/10.1007/s00204-019-02462-1

Alamer, M., Darbre, P.D., (2018). Effects of exposure to six chemical ultraviolet filters commonly used in personal care products on motility of MCF-7 and MDA-MB-231 human breast cancer cells *in vitro*. *Journal of Applied Toxicology*, 38, 148-159. https://doi.org/10.1002/jat.3525

Almeida, I.F., Pinto, A.S., Monteiro, C., Monteiro, H., Belo, L., Fernandes, J., Bento, A.R., Duarte, T.L., Garrido, J., Bahia, M.F., Sousa Lobo, J.M., Costa, P.C., (2015). Protective effect of *C. sativa* leaf extract against UV mediated-DNA damage in a human keratinocyte cell line. *Journal of Photochemistry and Photobiology B: Biology*,144, 28-34. https://doi.org/10.1016/j.jphotobiol.2015.01.010

Alonso, M.B., Feo, M.L., Corcellas, C., Gago-Ferrero, P., Bertozzi, C.P., Marigo, J., Flach, L., Meirelles, A.C.O., Carvalho, V.L., Azevedo, A.F., Torres, J.P.M., Lailson-Brito, J., Malm, O., Diaz-Cruz, M.S., Eljarrat, E., Barceló, D., (2015). Toxic heritage: maternal transfer of pyrethroid insecticides and sunscreen agents in dolphins from Brazil. *Environmental Pollution*, 207, 391-402. https://doi.org/10.1016/j.envpol.2015.09.039

Anway, M.D., Skinner, M.K., (2006). Epigenetic transgenerational actions of endocrine disruptors. *Endocrinology*, 147, S43-S49. https://doi.org/10.1210/en.2005-1058

Badia-Fabregat, M., Rodríguez-Rodríguez, C.E., Gago-Ferrero, P., Olivares, A., Piña, B., Díaz-Cruz, M.S., Vicent, T., Barceló, D., Caminal, G., (2012). Degradation of UV filters in sewage sludge and 4-MBC in liquid medium by the ligninolytic fungus *Trametes versicolor*. *Journal of Environmental Management*, 104, 114-120. https://doi.org/10.1016/j.jenvman.2012.03.039

Bakir, A., Rowland, S.J., Thompson, R.C., (2014). Transport of persistent organic pollutants by microplastics in estuarine conditions. *Estuarine, Coastal and Shelf Science*, 140, 14-21. https://doi.org/10.1016/j.ecss.2014.01.004

Balmer, M.E., Buser, H.R., Müller, M.D., Poiger, T., (2005). Occurrence of some organic UV filters in wastewater, in surface waters, and in fish from Swiss lakes. *Environmental Science and Technology*, 39, 953-962. https://doi.org/10.1021/es040055r

Ben-Zvi, O., Eyal, G., Loya, Y., (2015). Light-dependent fluorescence in the coral *Galaxea fascicularis*. *Hydrobiologia*, 759, 15-26. https://doi.org/10.1007/s10750-014-2063-6

Blüthgen, N., Zucchi, S., Fent, K., (2012). Effects of the UV filter benzophenone-3 (oxybenzone) at low concentrations in zebrafish (*Danio rerio*). *Toxicology and Applied Pharmacology*, 263, 184-194. https://doi.org/10.1016/j.taap.2012.06.008

Bundschuh, M., Filser, J., Lüderwald, S., McKee, M.S., Metreveli, G., Schaumann, G.E., Schulz, R., Wagner, S., (2018). Nanoparticles in the environment: where do we come from, where do we go to? *Environmental Sciences Europe*, 30, 1-17.

https://doi.org/10.1186/s12302-018-0132-6

Burkhardt-Holm, P., N'Guyen, A., (2019). Ingestion of microplastics by fish and other prey organisms of cetaceans, exemplified for two large baleen whale species. *Marine Pollution Bulletin*, 144, 224-234. https://doi.org/10.1016/j.marpolbul.2019.04.068

Cadena-Aizaga, M.I., Montesdeoca-Esponda, S., Torres-Padrón, M.E., Sosa-Ferrera, Z., Santana-Rodríguez, J.J., (2020). Organic UV filters in marine environments: An update of analytical methodologies, occurrence and distribution. *Trends in Environmental Analytical Chemistry*, 25, e00079. https://doi.org/10.1016/j.teac.2019.e00079

Calafat, A.M., Wong, L.Y., Ye, X., Reidy, J.A., Needham, L.L., (2008). Concentrations of the sunscreen agent benzophenone-3 in residents of the United States: National Health and Nutrition Examination Survey 2003-2004. *Environmental Health Perspectives*, 116, 893-897. https://doi.org/10.1289/ehp.11269

Cavus, I., Pan, J.W., Hetherington, H.P., Abi-Saab, W., Zaveri, H.P., Vives, K.P., Krystal, J.H., Spencer, S.S., Spencer, D.D., (2008). Decreased hippocampal volume on MRI is associated with increased extracellular glutamate in epilepsy patients. *Epilepsia*, 49, 1358-1366. https://doi.org/10.1111/j.1528-1167.2008.01603.x

Chen, Y., Vymazal, J., Březinová, T., Koželuh, M., Kule, L., Huang, J., Chen, Z., (2016). Occurrence, removal and environmental risk assessment of pharmaceuticals and personal care products in rural wastewater treatment wetlands. *Science of the Total Environment*, 566, 1660-1669. https://doi.org/10.1016/j.scitotenv.2016.06.069

Commission Regulation (2017). 2017/238 of 10 February 2017 amending Annex VI to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products, 37-38.

Corinaldesi, C., Marcellini, F., Nepote, E., Damiani, E., Danovaro, R., (2018). Impact of inorganic

UV filters contained in sunscreen products on tropical stony corals (*Acropora* spp.). *Science of the Total Environment*, 637, 1279-1285. https://doi.org/10.1016/j.scitotenv.2018.05.108

Courtene-Jones, W., Quinn, B., Gary, S.F., Mogg, A.O.M., Narayanaswamy, B.E., (2017). Microplastic pollution identified in deep-sea water and ingested by benthic invertebrates in the Rockall Trough, North Atlantic Ocean. *Environmental Pollution*, 231, 271-280. https://doi.org/10.1016/j.envpol.2017.08.026

Cozzi, A.C., Perugini, P., Gourion-Arsiquaud, S., (2018). Comparative behavior between sunscreens based on free or encapsulated UV filters in term of skin penetration, retention and photo-stability. *European Journal of Pharmaceutical Sciences*, 121, 309-318. https://doi.org/10.1016/j.ejps.2018.06.001

da Silva, A.C.P., Santos, B.A.M.C., Castro, H.C., Rodrigues, C.R., (2021). Ethylhexyl methoxycinnamate and butyl methoxydibenzoylmethane: toxicological effects on marine biota and human concerns. *Journal of Applied Toxicology*. https://doi.org/10.1002/jat.4210

Dauvergne, P., (2018). The power of environmental norms: marine plastic pollution and the politics of microbeads. *Environmental Politics*, 27, 579-597. https://doi.org/10.1080/09644016.2018.1449090

Díaz-Cruz, M.S., Barceló, D., (2009). Chemical analysis and ecotoxicological effects of organic UV-absorbing compounds in aquatic ecosystems. *TrAC - Trends in Analytical Chemistry*, 28, 708-717. https://doi.org/10.1016/j.trac.2009.03.010

Domínguez-Morueco, N., Moreno-Merino, L., Molins-Delgado, D., Díaz-Cruz, M.S., Aznar-Alemany, Ò., Eljarrat, E., Farré, M., López-Martínez, J., López de Alda, M., Silva, A., Durán Valsero, J.J., Valcárcel, Y., (2021). Anthropogenic contaminants in freshwater from the northern Antarctic Peninsula region. *Ambio*, 50, 544-559.

https://doi.org/10.1007/s13280-020-01404-x

Donohue, M.J., Masura, J., Gelatt, T., Ream, R., Baker, J.D., Faulhaber, K., Lerner, D.T., (2019). Evaluating exposure of northern fur seals, *Callorhinus ursinus*, to microplastic pollution through fecal analysis. *Marine Pollution Bulletin*, 138, 213-221. https://doi.org/10.1016/j.marpolbul.2018.11.036

Downs, C.A., Kramarsky-Winter, E., Fauth, J.E., Segal, R., Bronstein, O., Jeger, R., Lichtenfeld, Y., Woodley, C.M., Pennington, P., Kushmaro, A., Loya, Y., (2014). Toxicological effects of the sunscreen UV filter, benzophenone-2, on planulae and *in vitro* cells of the coral, *Stylophora pistillata*. *Ecotoxicology*, 23, 175-191. https://doi.org/10.1007/s10646-013-1161-y

Downs, C.A., Kramarsky-Winter, E., Segal, R., Fauth, J., Knutson, S., Bronstein, O., Ciner, F.R., Jeger, R., Lichtenfeld, Y., Woodley, C.M., Pennington, P., Cadenas, K., Kushmaro, A., Loya, Y., (2016). Toxicopathological effects of the sunscreen UV filter, oxybenzone (benzophenone-3), on coral planulae and cultured primary cells and Its environmental contamination in Hawaii and the U.S. Virgin Islands. *Archives of Environmental Contamination and Toxicology*, 70, 265-288. https://doi.org/10.1007/s00244-015-0227-7

Du, Y., Wang, W.Q., Pei, Z.T., Ahmad, F., Xu, R.R., Zhang, Y.M., Sun, L.W., (2017). Acute toxicity and ecological risk assessment of benzophenone-3 (BP-3) and benzophenone-4 (BP-4) in ultraviolet (UV)-filters. *International Journal of Environmental Research and Public Health*, 14, 1414. https://doi.org/10.3390/ijerph14111414

Ebele, A.J., Abou-Elwafa Abdallah, M., Harrad, S., (2017). Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. *Emerging Contaminants*, 3, 1-16. https://doi.org/10.1016/j.emcon.2016.12.004

Ekpeghere, K.I., Kim, U.J., O, S.H., Kim, H.Y., Oh, J.E., (2016). Distribution and seasonal occurrence of UV filters in rivers and wastewater treatment plants in Korea. *Science of the Total Environment*, 542, 121-128. https://doi.org/10.1016/j.scitotenv.2015.10.033

Fagervold, S.K., Rohée, C., Rodrigues, A.M.S., Stien, D. and Lebaron, P., 2021. Efficient degradation of the organic UV filter benzophenone-3 by *Sphingomonas wittichii* strain BP14P isolated from WWTP sludge. Science of the Total Environment, 758, 143674.

Faria, M., Navas, J.M., Soares, A.M.V.M., Barata, C., (2014). Oxidative stress effects of titanium dioxide nanoparticle aggregates in zebrafish embryos. *Science of the Total Environment*, 470, 379-389. https://doi.org/10.1016/j.scitotenv.2013.09.055

Fent, K., Zenker, A., Rapp, M., (2010). Widespread occurrence of estrogenic UV-filters in aquatic ecosystems in Switzerland. *Environmental Pollution*, 158, 1817-1824. https://doi.org/10.1016/j.envpol.2009.11.005

Ferguson, K.K., Meeker, J.D., Cantonwine, D.E., Mukherjee, B., Pace, G.G., Weller, D., McElrath, T.F., (2018). Environmental phenol associations with ultrasound and delivery measures of fetal growth. *Environment International*, 112, 243-250. https://doi.org/10.1016/j.envint.2017.12.011

Foot, N., Henshall, T., Kumar, S., (2017). Ubiquitination and the regulation of membrane proteins. *Physiological Reviews*, 97, 253-281. https://doi.org/10.1152/physrev.00012.2016

Gago-Ferrero, P., Alonso, M.B., Bertozzi, C.P., Marigo, J., Barbosa, L., Cremer, M., Secchi, E.R., Azevedo, A., Lailson-Brito, J., Torres, J.P.M., Malm, O., Eljarrat, E., Díaz-Cruz, M.S., Barceló, D., (2013). First determination of UV filters in marine mammals. octocrylene levels in Franciscana dolphins. *Environmental Science and Technology*, 47, 5619-5625. https://doi.org/10.1021/es400675y

Gago-Ferrero, P., Badia-Fabregat, M., Olivares, A., Piña, B., Blánquez, P., Vicent, T., Caminal, G., Díaz-Cruz, M.S., Barceló, D., (2012). Evaluation of fungal- and photo-degradation as potential treatments for the removal of sunscreens BP3 and BP1. *Science of the Total Environment*, 427, 355-363. https://doi.org/10.1016/j.scitotenv.2012.03.089

Gago-Ferrero, P., Díaz-Cruz, M.S., Barceló, D., (2011). Fast pressurized liquid extraction with in-cell purification and analysis by liquid chromatography tandem mass spectrometry for the determination of UV filters and their degradation products in sediments. *Analytical and Bioanalytical Chemistry*, 400, 2195-2204. https://doi.org/10.1007/s00216-011-4951-1

Gingerich, S., Kim, G.L., Chalmers, J.A., Koletar, M.M., Wang, X., Wang, Y., Belsham, D.D., (2010). Estrogen receptor alpha and G-protein coupled receptor 30 mediate the neuroprotective effects of 17β-estradiol in novel murine hippocampal cell models. *Neuroscience*, 170, 54-66. https://doi.org/10.1016/j.neuroscience.2010.06.076

Gobierno Aruba (2020) Environmental unfriendly products will be banned starting July 1,2020, retrieved November 5th, 2021, from https://www.government.aw/news/news_47033/item/environmental-unfriendly-products-will-be-banned-starting-july-1-2020_51844.html

Gondikas, A.P., Von Der Kammer, F., Reed, R.B., Wagner, S., Ranville, J.F., Hofmann, T., (2014). Release of TiO2 nanoparticles from sunscreens into surface waters: a one-year survey at the old danube recreational lake. *Environmental Science and Technology*, 48, 5415-5422. https://doi.org/10.1021/es405596y

Gonzalez, H., Farbrot, A., Larkö, O., Wennberg, A.M., (2006). Percutaneous absorption of the sunscreen benzophenone-3 after repeated whole-body applications, with and without ultraviolet irradiation. *British Journal of Dermatology*, 154, 337-340. https://doi.org/10.1111/j.1365-2133.2005.07007.x

Gottschalk, F., Lassen, C., Kjoelholt, J., Christensen, F., Nowack, B., (2015). Modeling flows and concentrations of nine engineered nanomaterials in the Danish environment. *International*

Journal of Environmental Research and Public Health, 12, 5581-5602. https://doi.org/10.3390/ijerph120505581

Haynes, V.N., Ward, J.E., Russell, B.J., Agrios, A.G., (2017). Photocatalytic effects of titanium dioxide nanoparticles on aquatic organisms—current knowledge and suggestions for future research. *Aquatic Toxicology*, 185, 138-148. https://doi.org/10.1016/j.aquatox.2017.02.012

Hernandez-Milian, G., Lusher, A., MacGabban, S., Rogan, E., (2019). Microplastics in grey seal (Halichoerus grypus) intestines: are they associated with parasite aggregations? *Marine Pollution Bulletin*, 146, 349-354. https://doi.org/10.1016/j.marpolbul.2019.06.014

Hewitt, N.J., Grégoire, S., Cubberley, R., Duplan, H., Eilstein, J., Ellison, C., Lester, C., Fabian, E., Fernandez, J., Géniès, C., Jacques-Jamin, C., Klaric, M., Rothe, H., Sorrell, I., Lange, D., Schepky, A., (2020). Measurement of the penetration of 56 cosmetic relevant chemicals into and through human skin using a standardized protocol. *Journal of Applied Toxicology*, 40, 403-405. https://doi.org/10.1002/jat.3913

Hopkins, Z.R., Blaney, L., (2016). An aggregate analysis of personal care products in the environment: identifying the distribution of environmentally-relevant concentrations. *Environment International*, 92, 301-316. https://doi.org/10.1016/j.envint.2016.04.026

Hopkins, Z.R., Snowberger, S., Blaney, L., (2017). Ozonation of the oxybenzone, octinoxate, and octocrylene UV-filters: reaction kinetics, absorbance characteristics, and transformation products. *Journal of Hazardous Materials*, 338, 338, 23-32. https://doi.org/10.1016/j.jhazmat.2017.05.016

Hu, C., Hou, J., Zhu, Y., Lin, D., (2020). Multigenerational exposure to TiO2 nanoparticles in soil stimulates stress resistance and longevity of survived *C. elegans* via activating insulin/IGF-like signaling. *Environmental Pollution*, 263, 114376. https://doi.org/10.1016/j.envpol.2020.114376

Huang, Y., Wang, P., Law, J.C.F., Zhao, Y., Wei, Q., Zhou, Y., Zhang, Y., Shi, H., Leung, K.S.Y., (2020). Organic UV filter exposure and pubertal development: a prospective follow-up study of urban Chinese adolescents. *Environment International*, 143, 105961. https://doi.org/10.1016/j.envint.2020.105961

Huo, W., Cai, P., Chen, M., Li, H., Tang, J., Xu, C., Zhu, D., Tang, W., Xia, Y., (2016). The relationship between prenatal exposure to BP-3 and Hirschsprung's disease. *Chemosphere*, 144, 1091-1097. https://doi.org/10.1016/j.chemosphere.2015.09.019

Iwasaki, S., Isobe, A., Kako, S., Uchida, K., Tokai, T., (2017). Fate of microplastics and mesoplastics carried by surface currents and wind waves: a numerical model approach in the Sea of Japan. *Marine Pollution Bulletin*, 121, 85-96. https://doi.org/10.1016/j.marpolbul.2017.05.057

Ji, J., Kakade, A., Yu, Z., Khan, A., Liu, P., Li, X., (2020). Anaerobic membrane bioreactors for treatment of emerging contaminants: a review. *Journal of Environmental Management*, 270, 110913. https://doi.org/10.1016/j.jenvman.2020.110913

Jones, J., Porter, A., Muñoz-pérez, J., Alarcón-ruales, D., Galloway, T., (2021). Plastic contamination of the Galapagos marine food web and the relative risks to native species. *Science of The Total Environment, 789, 147704. https://doi.org/10.1016/j.scitotenv.2021.147704*

Justus, C.R., Leffler, N., Ruiz-Echevarria, M., Yang, L. V., (2014). In vitro cell migration and invasion assays. *Journal of Visualized Experiments*, 88, 51046. https://doi.org/10.3791/51046

Kalčíková, G., Alič, B., Skalar, T., Bundschuh, M., Gotvajn, A.Ž., (2017). Wastewater treatment plant effluents as source of cosmetic polyethylene microbeads to freshwater. *Chemosphere*, 188, 25-31. https://doi.org/10.1016/j.chemosphere.2017.08.131

Karlsson, T.M., Vethaak, A.D., Almroth, B.C., Ariese, F., van Velzen, M., Hassellöv, M., Leslie, H.A., (2017). Screening for microplastics in sediment, water, marine invertebrates and fish: Method development and microplastic accumulation. *Marine Pollution Bulletin*, 122, 403-408. https://doi.org/10.1016/j.marpolbul.2017.06.081

Kentin, E., Kaarto, H., (2018). An EU ban on microplastics in cosmetic products and the right to regulate. *Review of European, Comparative and International Environmental Law*, 27, 254-266. https://doi.org/10.1111/reel.12269

Khan, N.A., Khan, S.U., Ahmed, S., Farooqi, I.H., Yousefi, M., Mohammadi, A.A., Changani, F., (2020). Recent trends in disposal and treatment technologies of emerging-pollutants- A critical review. *TrAC - Trends in Analytical Chemistry*, 122, 115744. https://doi.org/10.1016/j.trac.2019.115744

Khatmullina, L., Isachenko, I., (2017). Settling velocity of microplastic particles of regular shapes. *Marine Pollution Bulletin*, 114, 871-880. https://doi.org/10.1016/j.marpolbul.2016.11.024

Kidd, K.A., Blanchfield, P.J., Mills, K.H., Palace, V.P., Evans, R.E., Lazorchak, J.M., Flick, R.W., (2007). Collapse of a fish population after exposure to a synthetic estrogen. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 8897-8901. https://doi.org/10.1073/pnas.0609568104

Kim, K.B., Kim, Y.W., Lim, S.K., Roh, T.H., Bang, D.Y., Choi, S.M., Lim, D.S., Kim, Y.J., Baek, S.H., Kim, M.K., Seo, H.S., Kim, M.H., Kim, H.S., Lee, J.Y., Kacew, S., Lee, B.M., (2017). Risk assessment of zinc oxide, a cosmetic ingredient used as a UV filter of sunscreens. *Journal of Toxicology and Environmental Health - Part B: Critical Reviews*, 20, 155-182. https://doi.org/10.1080/10937404.2017.1290516

Koopman-Verhoeff, M.E., Gredvig-Ardito, C., Barker, D.H., Saletin, J.M., Carskadon, M.A., (2020). Classifying pubertal development using child and parent report: comparing the pubertal development scales to tanner staging. *Journal of Adolescent Health*, 66, 597-602. https://doi.org/10.1016/j.jadohealth.2019.11.308

Kowalski, N., Reichardt, A.M., Waniek, J.J., (2016). Sinking rates of microplastics and potential implications of their alteration by physical, biological, and chemical factors. *Marine Pollution Bulletin*, 109, 310-319. https://doi.org/10.1016/j.marpolbul.2016.05.064

Krause, M., Frederiksen, H., Sundberg, K., Jørgensen, F.S., Jensen, L.N., Nørgaard, P., Jørgensen, C., Ertberg, P., Juul, A., Drzewiecki, K.T., Skakkebaek, N.E., Andersson, A.M., (2018). Presence of benzophenones commonly used as UV filters and absorbers in paired maternal and fetal samples. *Environment International*, 110, 51-60. https://doi.org/10.1016/j.envint.2017.10.005

Kyaw, B.M., Champakalakshmi, R., Sakharkar, M.K., Lim, C.S., Sakharkar, K.R., (2012). Biodegradation of low density polythene (LDPE) by *Pseudomonas* species. *Indian Journal of Microbiology*, 52, 411-419. https://doi.org/10.1007/s12088-012-0250-6

Labille, J., Slomberg, D., Catalano, R., Robert, S., Apers-Tremelo, M.L., Boudenne, J.L., Manasfi, T., Radakovitch, O., (2020). Assessing UV filter inputs into beach waters during recreational activity: A field study of three French Mediterranean beaches from consumer survey to water analysis. *Science of the Total Environment*, 706, 136010. https://doi.org/10.1016/j.scitotenv.2019.136010

Lai, W.W.P., Chen, K.L., Lin, A.Y.C., (2020). Solar photodegradation of the UV filter 4-methylbenzylidene camphor in the presence of free chlorine. *Science of the Total Environment*, 722, 137860. https://doi.org/10.1016/j.scitotenv.2020.137860

Lam, C.S., Ramanathan, S., Carbery, M., Gray, K., Vanka, K.S., Maurin, C., Bush, R., Palanisami, T., (2018). A comprehensive analysis of plastics and microplastic legislation worldwide. *Water, Air, and Soil Pollution*, 229, 1-19. https://doi.org/10.1007/s11270-018-4002-z

Leiter, U., Keim, U., Garbe, C., (2020). Epidemiology of skin cancer: Update 2019. In Jörg Reichrath (Ed), *Sunlight, Vitamin D and Skin Cancer* (pp. 123-139). Springer. https://doi.org/10.1007/978-3-030-46227-7_6

Li, V.W.T., Tsui, M.P.M., Chen, X., Hui, M.N.Y., Jin, L., Lam, R.H.W., Yu, R.M.K., Murphy, M.B., Cheng, J., Lam, P.K.S., Cheng, S.H., (2016). Effects of 4-methylbenzylidene camphor (4-MBC) on neuronal and muscular development in zebrafish (*Danio rerio*) embryos. *Environmental Science and Pollution Research*, 23, 8275-8285. https://doi.org/10.1007/s11356-016-6180-9

Lim, C.L., Koh, R.Y., Haw, T.Y., Boudville, L.A., (2015). Antioxidant Activity of the Sea Bird Nest (Eucheuma Cottonii) and Its Radical Scavenging Effect on Human Keratinocytes. *Journal of Medical and Bioengineering*, 4, 461-465. https://doi.org/10.12720/jomb.4.6.461-465

Liu, L., Lou, J., Fu, Q., (2016). Fas, Bcl-2, and Caspase-3 Protein and Morphine Addiction. *Neuropathology of Drug Addictions and Substance Misuse,* 3, 517-524. https://doi.org/10.1016/B978-0-12-800634-4.00052-4

Liu, Y.S., Ying, G.G., Shareef, A., Kookana, R.S., (2011). Photostability of the UV filter benzophenone-3 and its effect on the photodegradation of benzotriazole in water. *Environmental Chemistry*, 8, 581-588. https://doi.org/10.1071/EN11068

Lu, D., Qu, Y., Shi, F., Feng, D., Tao, K., Gao, G., He, S., Zhao, T., (2016). Activation of G protein-coupled estrogen receptor 1 (GPER-1) ameliorates blood-brain barrier permeability after global cerebral ischemia in ovariectomized rats. *Biochemical and Biophysical Research Communications*, 477, 209-214. https://doi.org/10.1016/j.bbrc.2016.06.044

Lusher, A.L., Tirelli, V., O'Connor, I., Officer, R., (2015). Microplastics in Arctic polar waters: the first reported values of particles in surface and sub-surface samples. *Scientific Reports*, 5, 1-9. https://doi.org/10.1038/srep14947

Mahlalela, L.C., Ngila, J.C., Dlamini, L.N., (2017). Monitoring the fate and behavior of TiO2 nanoparticles: simulated in a WWTP with industrial dye-stuff effluent according to OECD 303A. *Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering*, 52, 794-803. https://doi.org/10.1080/10934529.2017.1305176

Mao, F., He, Y., Kushmaro, A., Gin, K.Y.H., (2017). Effects of benzophenone-3 on the green alga *Chlamydomonas reinhardtii* and the cyanobacterium *Microcystis aeruginosa. Aquatic Toxicology*, 193, 1-8. https://doi.org/10.1016/j.aquatox.2017.09.029

Matta, M.K., Florian, J., Zusterzeel, R., Pilli, N.R., Patel, V., Volpe, D.A., Yang, Y., Oh, L., Bashaw, E., Zineh, I., Sanabria, C., Kemp, S., Godfrey, A., Adah, S., Coelho, S., Wang, J., Furlong, L.A., Ganley, C., Michele, T., Strauss, D.G., (2020). Effect of sunscreen application on plasma concentration of sunscreen active ingredients: a randomized clinical trial. *Journal of the American Medical Association*, 323, 256-267. https://doi.org/10.1001/jama.2019.20747

Meinds, R.J., van der Steeg, A.F.W., Sloots, C.E.J., Witvliet, M.J., de Blaauw, I., van Gemert, W.G., Trzpis, M., Broens, P.M.A., (2019). Long-term functional outcomes and quality of life in patients with Hirschsprung's disease. *British Journal of Surgery*, 106, 499-507. https://doi.org/10.1002/bjs.11059

Minetto, D., Libralato, G., Marcomini, A., Volpi Ghirardini, A., (2017). Potential effects of TiO2 nanoparticles and TiCl4 in saltwater to *Phaeodactylum tricornutum* and *Artemia franciscana*. *Science of the Total Environment*, 579, 1379-1386. https://doi.org/10.1016/j.scitotenv.2016.11.135

Molins-Delgado, D., Olmo-Campos, M. del M., Valeta-Juan, G., Pleguezuelos-Hernández, V., Barceló, D., Díaz-Cruz, M.S., (2018). Determination of UV filters in human breast milk using turbulent flow chromatography and babies' daily intake estimation. *Environmental Research*, 161, 532-539. https://doi.org/10.1016/j.envres.2017.11.033

Molins-Delgado, D., Távora, J., Silvia Díaz-Cruz, M., Barceló, D., (2017). UV filters and benzotriazoles in urban aquatic ecosystems: the footprint of daily use products. *Science of the Total Environment*, 601, 975-986. https://doi.org/10.1016/j.scitotenv.2017.05.176

Moore, R.C., Loseto, L., Noel, M., Etemadifar, A., Brewster, J.D., MacPhee, S., Bendell, L., Ross, P.S., (2020). Microplastics in beluga whales (*Delphinapterus leucas*) from the Eastern Beaufort Sea. *Marine Pollution Bulletin*, 150, 110723. https://doi.org/10.1016/j.marpolbul.2019.110723

Morlando, A., Cardillo, D., Devers, T., Konstantinov, K., (2016). Titanium doped tin dioxide as potential UV filter with low photocatalytic activity for sunscreen products. *Materials Letters*, 171, 289-292. https://doi.org/10.1016/j.matlet.2016.02.094

Nagler, J.J., Davis, T.L., Modi, N., Vijayan, M.M., Schultz, I., (2010). Intracellular, not membrane, estrogen receptors control vitellogenin synthesis in the rainbow trout. *General and Comparative Endocrinology*, 167, 326-330. https://doi.org/10.1016/j.ygcen.2010.03.022

Nakata, H., Murata, S., Shinohara, R., (2009). Occurrence and concentrations of persistent personal care products, organic UV filters, in the marine environment. *Interdisciplinary Studies in Environmental Chemistry*, 1, 239-246.

Narla, S., Lim, H.W., (2020). Sunscreen: FDA regulation, and environmental and health impact. *Photochemical and Photobiological Sciences*, 19, 66-70. https://doi.org/10.1039/c9pp00366e

Nava, V., Leoni, B., (2021). A critical review of interactions between microplastics, microalgae and aquatic ecosystem function. *Water Research*, 188, 116476. https://doi.org/10.1016/j.watres.2020.116476

Neal, C., Jarvie, H., Rowland, P., Lawler, A., Sleep, D., Scholefield, P., (2011). Titanium in UK rural, agricultural and urban/industrial rivers: geogenic and anthropogenic colloidal/sub-colloidal sources and the significance of within-river retention. *Science of the Total Environment*, 409, 1843-1853. https://doi.org/10.1016/j.scitotenv.2010.12.021

O'Donovan, S., Mestre, N.C., Abel, S., Fonseca, T.G., Carteny, C.C., Willems, T., Prinsen, E., Cormier, B., Keiter, S.S., Bebianno, M.J., (2020). Effects of the UV filter, oxybenzone, adsorbed to microplastics in the clam Scrobicularia plana. *Science of the Total Environment*, 733, 139102. https://doi.org/10.1016/j.scitotenv.2020.139102

Osterwalder, U., Sohn, M., Herzog, B., (2014). Global state of sunscreens. *Photodermatology Photoimmunology and Photomedicine*, 30, 62-80. https://doi.org/10.1111/phpp.12112

Paredes, E., Perez, S., Rodil, R., Quintana, J.B., Beiras, R., (2014). Ecotoxicological evaluation of four UV filters using marine organisms from different trophic levels *Isochrysis galbana*, *Mytilus galloprovincialis*, *Paracentrotus lividus*, and *Siriella armata*. *Chemosphere*, 104, 44-50. https://doi.org/10.1016/j.chemosphere.2013.10.053

Philippat, C., Mortamais, M., Chevrier, C., Petit, C., Calafat, A.M., Ye, X., Silva, M.J., Brambilla, C., Pin, I., Charles, M.A., Cordier, S., Slama, R., 2012. Exposure to phthalates and phenols during pregnancy and offspring size at birth. *Environmental Health Perspectives*, 120, 464-470. https://doi.org/10.1289/ehp.1103634

Pomierny, B., Krzyzanowska, W., Broniowska, Z., Strach, B., Bystrowska, B., Starek-Zwiechowicz, B., Maciejska, A., Skórkowska, A., Wesolowska, J., Walczak, M., Budziszewska, B., (2019). Benzophenone-3 passes through the blood-brain barrier, increases the level of extracellular glutamate, and induces apoptotic processes in the hippocampus and frontal cortex of rats. *Toxicological Sciences*, 171, 485-500. https://doi.org/10.1093/toxsci/kfz160

Rainieri, S., Conlledo, N., Larsen, B.K., Granby, K., Barranco, A., (2018). Combined effects of microplastics and chemical contaminants on the organ toxicity of zebrafish (*Danio rerio*). *Environmental Research*, 162, 135-142. https://doi.org/10.1016/j.envres.2017.12.019

Republic of Palau (2018), Office of the President, ***The Responsible Tourism Education Act of 2018***, retrieved on November 5th, 2021, from https://www.palaugov.pw/wp-content/uploads/2018/10/RPPL-No.-10-30-re.-Responsible-Tourism-Education-Act-of-2018.pdf

Reisser, J., Slat, B., Noble, K., Du Plessis, K., Epp, M., Proietti, M., De Sonneville, J., Becker, T., Pattiaratchi, C., (2015). The vertical distribution of buoyant plastics at sea: an observational study in the North Atlantic Gyre. *Biogeosciences*, 12, 1249-1256. https://doi.org/10.5194/bg-12-1249-2015

Rodil, R., Moeder, M., Altenburger, R., Schmitt-Jansen, M., (2009). Photostability and phytotoxicity of selected sunscreen agents and their degradation mixtures in water. *Analytical and Bioanalytical Chemistry*, 395, 1513-1524. https://doi.org/10.1007/s00216-009-3113-1

Roth, K.A., D'Sa, C., (2001). Apoptosis and brain development. *Mental Retardation and Developmental Disabilities Research Reviews*, 7, 261-266. https://doi.org/10.1002/mrdd.1036

Salthammer, T., (2020). Emerging indoor pollutants. *International Journal of Hygiene and Environmental Health*, 224, 113423. https://doi.org/10.1016/j.ijheh.2019.113423

Santamaría, C.G., Abud, J.E., Porporato, M.M., Meyer, N., Zenclussen, A.C., Kass, L., Rodríguez, H.A., (2019). The UV filter benzophenone 3, alters early follicular assembly in

rat whole ovary cultures. *Toxicology Letters*, 303, 48-54.
https://doi.org/10.1016/j.toxlet.2018.12.016

Schaumann, G.E., Philippe, A., Bundschuh, M., Metreveli, G., Klitzke, S., Rakcheev, D., Grün, A., Kumahor, S.K., Kühn, M., Baumann, T., Lang, F., Manz, W., Schulz, R., Vogel, H.J., (2015). Understanding the fate and biological effects of Ag- and TiO2-nanoparticles in the environment: the quest for advanced analytics and interdisciplinary concepts. *Science of the Total Environment*, 535, 3-19. https://doi.org/10.1016/j.scitotenv.2014.10.035

Schlumpf, M., Jarry, H., Wuttke, W., Ma, R., Lichtensteiger, W., (2004). Estrogenic activity and estrogen receptor β binding of the UV filter 3-benzylidene camphor: Comparison with 4-methylbenzylidene camphor. *Toxicology*, 199, 109-120.
https://doi.org/10.1016/j.tox.2004.02.015

Schlumpf, M., Kypke, K., Wittassek, M., Angerer, J., Mascher, H., Mascher, D., Vökt, C., Birchler, M., Lichtensteiger, W., (2010). Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: Correlation of UV filters with use of cosmetics. *Chemosphere*, 81, 1171-1183.
https://doi.org/10.1016/j.chemosphere.2010.09.079

Schneider, S.L., Lim, H.W., (2019a). Review of environmental effects of oxybenzone and other sunscreen active ingredients. *Journal of the American Academy of Dermatology*, 80, 266-271. https://doi.org/10.1016/j.jaad.2018.06.033

Schneider, S.L., Lim, H.W., (2019b). A review of inorganic UV filters zinc oxide and titanium dioxide. *Photodermatology Photoimmunology and Photomedicine*, 35, 442-446.
https://doi.org/10.1111/phpp.12439

Sehar, S., Naz, I., (2016). Role of the biofilms in wastewater treatment. In Dharumadurai Dhanasekaran and Nooruddin Thajuddin (Eds.), *Microbial Biofilms - Importance and*

Applications (pp.121-144). IntechOpen. https://doi.org/10.5772/63499

Serpone, N., Dondi, D., Albini, A., (2007). Inorganic and organic UV filters: their role and efficacy in sunscreens and suncare products. *Inorganica Chimica Acta*, 360, 794-802. https://doi.org/10.1016/j.ica.2005.12.057

Soler de la Vega, A.C., Cruz-Alcalde, A., Mazón, C.S., Martí, C.B., Diaz-Cruz, M.S., (2021). Nano-TiO2 phototoxicity in fresh and seawater: *Daphnia magna* and *Artemia* sp. as proxies. *Water,* 13, 55. https://doi.org/10.3390/w13010055

Song, S., He, Y., Huang, Y., Huang, X., Guo, Y., Zhu, H., Kannan, K., Zhang, T., (2020). Occurrence and transfer of benzophenone-type ultraviolet filters from the pregnant women to fetuses. *Science of the Total Environment*, 726, 138503. https://doi.org/10.1016/j.scitotenv.2020.138503

Souza, C., Maia Campos, P.M.B.G., (2017). Development of a HPLC method for determination of four UV filters in sunscreen and its application to skin penetration studies. *Biomedical Chromatography*, 31, e4029. https://doi.org/10.1002/bmc.4029

Suleiman, M., Schröder, C., Kuhn, M., Simon, A., Stahl, A., Frerichs, H., Antranikian, G., (2019). Microbial biofilm formation and degradation of octocrylene, a UV absorber found in sunscreen. *Communications Biology*, 2, 1-5. https://doi.org/10.1038/s42003-019-0679-9

Szylberg, L., Marszalek, A., (2014). Diagnosis of Hirschsprung's disease with particular emphasis on histopathology. A systematic review of current literature. *Przeglad Gastroenterologiczny*, 9, 264. https://doi.org/10.5114/pg.2014.46160

Tang, R., Chen, M.J., Ding, G.D., Chen, X.J., Han, X.M., Zhou, K., Chen, L.M., Xia, Y.K., Tian, Y., Wang, X.R., (2013). Associations of prenatal exposure to phenols with birth outcomes. *Environmental Pollution*, 178, 115-120. https://doi.org/10.1016/j.envpol.2013.03.023

Tang, Y., Cai, R., Cao, D., Kong, X., Lu, Y., (2018). Photocatalytic production of hydroxyl radicals by commercial TiO2 nanoparticles and phototoxic hazard identification. *Toxicology*, 406, 1-8. https://doi.org/10.1016/j.tox.2018.05.010

Tapper, M.A., Denny, J.S., Serrano, J.A., Kolanczyk, R.C., Sheedy, B.R., Overend, G.M., Hornung, M.W., Schmieder, P.K., (2019). Phenone, hydroxybenzophenone, and branched phenone estrogen receptor binding and vitellogenin agonism in rainbow trout *in vitro* models. *Applied In Vitro Toxicology*, 5, 62-74. https://doi.org/10.1089/aivt.2018.0008

Thia, E., Chou, P.H., Chen, P.J., (2020). *In vitro* and *in vivo* screening for environmentally friendly benzophenone-type UV filters with beneficial tyrosinase inhibition activity. *Water Research*, 185, 116208. https://doi.org/10.1016/j.watres.2020.116208

Tsui, M.M.P., Leung, H.W., Wai, T.C., Yamashita, N., Taniyasu, S., Liu, W., Lam, P.K.S., Murphy, M.B., (2014). Occurrence, distribution and ecological risk assessment of multiple classes of UV filters in surface waters from different countries. *Water Research*, 67, 55-65. https://doi.org/10.1016/j.watres.2014.09.013

Van Der Meer, T.P., Artacho-Cordón, F., Swaab, D.F., Struik, D., Makris, K.C., Wolffenbuttel, B.H.R., Frederiksen, H., Van Vliet-Ostaptchouk, J. V., (2017). Distribution of non-persistent endocrine disruptors in two different regions of the human brain. *International Journal of Environmental Research and Public Health*, 14, 1059. https://doi.org/10.3390/ijerph14091059

Vasilachi, I.C., Asiminicesei, D.M., Fertu, D.I., Gavrilescu, M., (2021). Occurrence and fate of emerging pollutants in water environment and options for their removal. *Water*, 13, 181. https://doi.org/10.3390/w13020181

Vassalle, L., Sunyer-Caldú, A., Díaz-Cruz, M.S., Arashiro, L.T., Ferrer, I., Garfí, M., García-Galán, M.J., (2020). Behavior of UV filters, UV blockers and pharmaceuticals in high rate algal ponds treating urban wastewater. *Water*, 12, 2658.

https://doi.org/10.3390/w12102658

Vela-Soria, F., Jiménez-Díaz, I., Rodríguez-Gómez, R., Zafra-Gómez, A., Ballesteros, O., Navalón, A., Vílchez, J.L., Fernández, M.F., Olea, N., (2011). Determination of benzophenones in human placental tissue samples by liquid chromatography-tandem mass spectrometry. *Talanta*, 85, 1848-1855. https://doi.org/10.1016/j.talanta.2011.07.030

Vione, D., Calza, P., Galli, F., Fabbri, D., Santoro, V., Medana, C., (2015). The role of direct photolysis and indirect photochemistry in the environmental fate of ethylhexyl methoxy cinnamate (EHMC) in surface waters. *Science of the Total Environment*, 537, 58-68. https://doi.org/10.1016/j.scitotenv.2015.08.002

Wagemaker, T.A.L., Silva, S.A.M., Leonardi, G.R., Maia Campos, P.M.B.G., (2015). Green Coffea arabica L: Seed oil influences the stability and protective effects of topical formulations. *Industrial Crops and Products*, 63, 34-40. https://doi.org/10.1016/j.indcrop.2014.09.045

Wang, L., Asimakopoulos, A.G., Kannan, K., (2015). Accumulation of 19 environmental phenolic and xenobiotic heterocyclic aromatic compounds in human adipose tissue. *Environment International*, 78, 45-50. https://doi.org/10.1016/j.envint.2015.02.015

Wang, J., Nabi, M.M., Mohanty, S.K., Afrooz, A.N., Cantando, E., Aich, N., Baalousha, M., (2020). Detection and quantification of engineered particles in urban runoff. *Chemosphere*, 248, 126070. https://doi.org/10.1016/j.chemosphere.2020.126070

Wnuk, A., Kajta, M., 2017. Steroid and Xenobiotic Receptor Signalling in Apoptosis and Autophagy of the Nervous System. *International Journal of Molecular Sciences*, 18, 2394. https://doi.org/10.3390/ijms18112394

Wnuk, A., Rzemieniec, J., Litwa, E., Lasoń, W., Kajta, M., (2018). Prenatal exposure to benzophenone-3 (BP-3) induces apoptosis, disrupts estrogen receptor expression and alters the epigenetic status of mouse neurons. *Journal of Steroid Biochemistry and Molecular Biology* ,182, 106-108. https://doi.org/10.1016/j.jsbmb.2018.04.016

Wojciechowski, K., Zukowska, G.Z., Korczagin, I., Malanowski, P., (2015). Effect of TiO2 on UV stability of polymeric binder films used in waterborne facade paints. *Progress in Organic Coatings*, 85, 123-130. https://doi.org/10.1016/j.porgcoat.2015.04.002

Wolff, M.S., Engel, S.M., Berkowitz, G.S., Ye, X., Silva, M.J., Zhu, C., Wetmur, J., Calafat, A.M., (2008). Prenatal phenol and phthalate exposures and birth outcomes. *Environmental Health Perspectives*, 116, 1092-1097. https://doi.org/10.1289/ehp.11007

Wong, S.W.Y., Leung, P.T.Y., Djurišić, A.B., Leung, K.M.Y., (2010). Toxicities of nano zinc oxide to five marine organisms: influences of aggregate size and ion solubility. *Analytical and Bioanalytical Chemistry*, 396, 609-618. https://doi.org/10.1007/s00216-009-3249-z

Wu, C., Zhang, K., Huang, X., Liu, J., (2016). Sorption of pharmaceuticals and personal care products to polyethylene debris. *Environmental Science and Pollution Research*, 23, 8819-8826. https://doi.org/10.1007/s11356-016-6121-7

Xu, H., Yang, J., Wang, Y., Jiang, Q., Chen, H., Song, H., (2008). Exposure to 17α-ethynylestradiol impairs reproductive functions of both male and female zebrafish (*Danio rerio*). *Aquatic Toxicology*, 88, 1-8. https://doi.org/10.1016/j.aquatox.2008.01.020

Yamamoto, F.Y., Garcia, J.R.E., Kupsco, A., Oliveira Ribeiro, C.A., (2017). Vitellogenin levels and others biomarkers show evidences of endocrine disruption in fish species from Iguaçu River - Southern Brazil. *Chemosphere*, 186, 88-99. https://doi.org/10.1016/j.chemosphere.2017.07.111

Zhang, A.P., Sun, Y.P., (2004). Photocatalytic killing effect of TiO2 nanoparticles on Ls-174-t human colon carcinoma cells. *World Journal of Gastroenterology*, 10, 3191. https://doi.org/10.3748/wjg.v10.i21.3191

Zhang, P., Lu, G., Liu, J., Yan, Z., Dong, H., Zhou, R., (2021). Biodegradation of 2-ethylhexyl-4-methoxycinnamate in river sediments and its impact on microbial communities. *Journal of Environmental Sciences*,104, 307-316. https://doi.org/10.1016/j.jes.2020.12.013

Zhang, Q., Ma, X., Dzakpasu, M., Wang, X.C., (2017). Evaluation of ecotoxicological effects of benzophenone UV filters: luminescent bacteria toxicity, genotoxicity and hormonal activity. *Ecotoxicology and Environmental Safety* ,142, 338-347. https://doi.org/10.1016/j.ecoenv.2017.04.027

Zhang, Q.Y., Ma, X.Y., Wang, X.C., Ngo, H.H., (2016). Assessment of multiple hormone activities of a UV-filter (octocrylene) in zebrafish (*Danio rerio*). *Chemosphere*, 159, 433-441. https://doi.org/10.1016/j.chemosphere.2016.06.037

Zhao, S., Miao, D., Zhu, K., Tao, K., Wang, C., Sharma, V.K., Jia, H., (2019). Interaction of benzo[a]pyrene with Cu(II)-montmorillonite: generation and toxicity of environmentally persistent free radicals and reactive oxygen species. *Environment International*, 129, 154-163. https://doi.org/10.1016/j.envint.2019.05.037

Zhong, X., Downs, C.A., Li, Yuting, Zhang, Z., Li, Yiman, Liu, B., Gao, H., Li, Q., (2020). Comparison of toxicological effects of oxybenzone, avobenzone, octocrylene, and octinoxate sunscreen ingredients on cucumber plants (*Cucumis sativus* L.). *Science of the Total Environment*, 714, 136879. https://doi.org/10.1016/j.scitotenv.2020.136879

Zhou, F., Dong, H., Liu, Yaling, Yan, L., Sun, C., Hao, P., Liu, Yuanyuan, Zhai, J., Liu, Yakun, (2018). Raloxifene, a promising estrogen replacement, limits TDP-25 cell death by enhancing autophagy and suppressing apoptosis. *Brain Research Bulletin*, 140, 281-290. https://doi.org/10.1016/j.brainresbull.2018.05.017

Zhu, L., Wang, H., Chen, B., Sun, X., Qu, K., Xia, B., (2019). Microplastic ingestion in deep-sea

fish from the South China Sea. *Science of the Total Environment*, 677, 493-501.
https://doi.org/10.1016/j.scitotenv.2019.04.380