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Review

Potential Effects of Persistent Organic Contaminants on Marine Biota: A Review on Recent Research

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Abstract: Synthetic organic compounds belonging to different chemical classes and possessing diverse physicochemical properties are frequently present in marine environments. Microplastics, pharmaceuticals, pesticides, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons (PAHs) are contained in the list of persistent organic pollutants (POPs) that have been detected in the global marine system. Numerous ecotoxicological studies have revealed the direct and indirect effects of anthropogenic toxicants on marine biota. The present review presents the research that has been conducted during the period from 1 January 2016 to 30 June 2021 concerning the lethal and sub-lethal impacts of selected organic-synthetic stressors on different plant and animal marine species, and summarizes the observed or predicted individual and combined effects after exposure to chemical mixtures of such contaminants. Future research needs dependent on the knowledge gaps that remain in the bibliography are also highlighted.

Keywords: toxicity; impacts; bioassays; ecotoxicology; persistent organic pollutants; pesticides; pharmaceuticals; microplastics; marine organisms

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1. Introduction

A wide variety of anthropogenic synthetic compounds of organic nature that are used in terrestrial areas for several different purposes can penetrate the sea environment through different pathways and mechanisms (Figure 1). Therefore, large inputs of various man-made synthetic substances launch into the oceans. Plastics, plastic-derived chemicals, pharmaceuticals, drugs, pesticides, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons (PAHs) are only some examples contained in the list of persistent organic pollutants (POPs) that sometimes eventually reach the coastal and open-sea ecosystems even though they are considered toxic pollutants.

Those chemicals belong to different chemical classes and possess diverse physicochemical properties in terms of molecular size, hydrophobicity, ionic strength, polarity, volatility, and several other characteristics that determine the distribution, availability, and environmental persistence of their molecules in the marine ecosystems.

According to the relevant literature, numerous invisible and visible pollutants, either individual or contained in chemical mixtures, have the potential after their entrance into the ocean to travel for long distances and periods of time that are dependent on their persistence, bioavailability, mobility, and distribution into the different compartments of marine ecosystems (water column, sediment, and biota), and consequently cause impacts on a wide range of marine organisms many degrees of latitude and longitude away from their origin and their entrance to the sea system [1].

Figure 1. Sources and pathways for selected/studied categories of POPs into the marine environment.

Several different classes of POPs have been detected in the global marine system during the last years [2–6]. For instance, the detection of microplastic pollution in seawater and marine organisms in samples taken from the Tropical Eastern Pacific and the Galápagos archipelago has been reported in a recently published research of Alfaro-Núñez et al. (2021) [2]. The occurrence and spatial distribution of 158 pharmaceuticals, drugs of abuse and related metabolites in offshore seawater have been examined by Alygizakis et al. (2016) [4]. Similarly, the presence of antifouling biocides in aquatic systems including marine ecosystems has been investigated and reported in a newly reported investigation of de Campos et al. (2021) [6].

Subsequently, during the last decades an intense and stable scientific interest focusing on the potential biological effects of those toxicants towards non-target aquatic organisms of different trophic levels is observed in the published data. Numerous studies in the field of ecotoxicology have revealed the direct and indirect effects of anthropogenic toxicants on marine biota either on individual population, or community, or entire ecosystem level.

The current chapter aims: (i) to present and discuss the research that has been conducted concerning the lethal and sub-lethal impacts of selected organic-synthetic stressors on different plant and animal marine species, (ii) to summarize the observed or predicted combined effects after exposure to chemical mixtures of such contaminants based on the data published from 2016, and (iii) to highlight the future research needs depending on the knowledge gaps that may remain in the relevant bibliography.

2. Methods

The search was mainly conducted in the "Scopus Database", whereas the additional citations that were located by "Google Scholar", "SpringerLink", and "Open Access Journal Search Engine" were also added to the list of reviewed literature.

Several different combinations of keywords were used to collect both research and review papers from peer-reviewed journals published in the global scientific bibliography. Book chapters, conference papers, editorials, books, short surveys, notes, and letters were also included in the retrieved data. The specific search terms and keywords that were inserted in the "search" of the Scopus database included the name of each individual group of targeted POPs (either one of the categories microplastics, pharmaceuticals, pesticides, PCBs, or PAHs) and "marine toxicity", or "impacts on marine organisms", or "effects on marine biota", or "stress on marine organisms". In this point, it must be mentioned that only the studies that were published during the period from 1 January 2016 to 30 June 2021 were collected and reviewed, whereas the total number of found data was 4272 documents.

Afterward, the obtained data were characterized as relevant or irrelevant on the basis of the scope of each study as described and presented by their authors in the abstract. Irrelevant studies were excluded. Next, based on the further information of the accepted surveys as contained in the extended articles of the studies concerning the impacts of selected POPs towards marine organisms, the relevant studies were categorized into five main categories: (i) microplastics and plastic-derived organics, (ii) pharmaceuticals, (iii) pesticides, (iv) PCBs, and (v) PAHs. Each one of the aforementioned categories was further subdivided into three subgroups that were named (a) experimental, (b) nonexperimental/prediction models, and (c) reviews.

3. Review Results

According to the findings of the current review, a great number of publications have arisen by researchers in the last 5.5 years regarding the evaluation of the ecotoxicological impacts of five selected groups of persistent organic pollutants towards the exposed flora and fauna inhabitants of marine ecosystems that receive their inputs. Based on the gathered and categorized data, depicted in Figure 2, it is indicated that the majority of the studies (≈28%) is dealing with the group of pharmaceuticals, followed by pesticides/agrochemicals (≈24%), PAHs (≈21%), microplastics and plastic-derived chemicals (≈17%), and PCBs (≈10%).

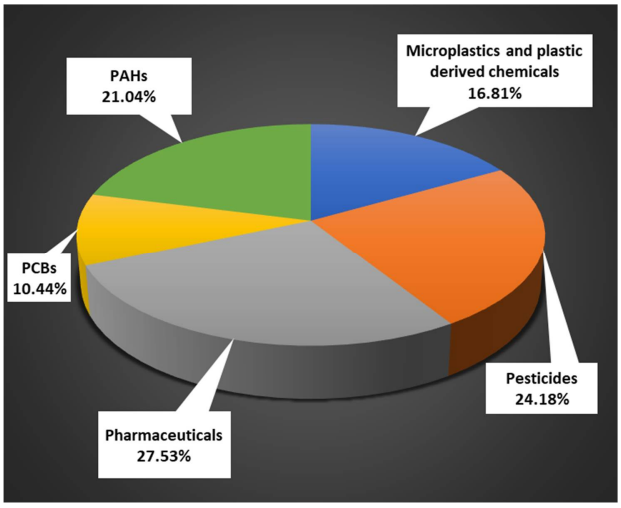

Figure 2. Overall relative frequency of reports of different chemical groups of POPs overviewed in present review regarding the evaluation of their potential toxicity on marine biota. The plotted data were obtained from "Scopus", "Google Scholar", "SpringerLink", and "Open Access Journal Search Engine". Overall means all kinds of data including research article, review, short notes, editorial commentary, research articles, books and book chapters, etc., that were published from 1 January 2016 to 30 June 2021. Target pollutants were tested either individually or in mixture with other contaminants.

Figure 3 depicts the annual number of records published for each selected chemical group of reviewed pollutants in which a constantly growing number of studies regarding the effects of several types and sizes of microplastics (MPs), nanoplastics (NPs), and plastic-derived chemicals is observed. Moreover, in this point, it must be underlined the fact that even if the survey for 2021 is restricted only to the first half of the year (from 1 January 2021 to 30 June 2021), a large number of retrieved data is observed, indicating the enlarged scientific interest in the ecotoxicological impacts of selected POPs.

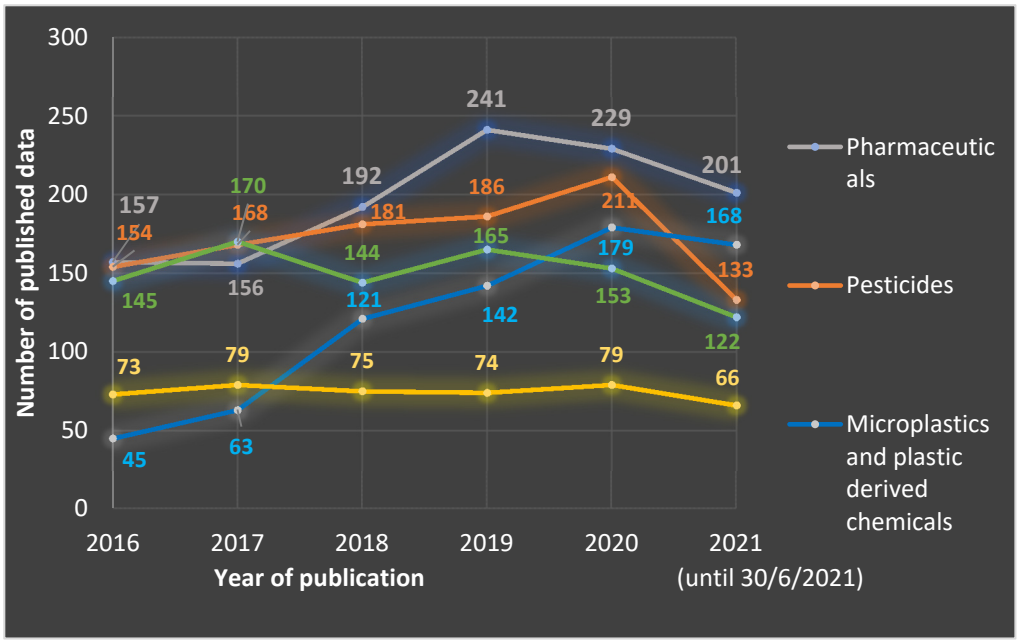

Figure 3. Annual number of records published for each selected chemical group of POPs and potential effects on marine biota. The plotted data were obtained from "Scopus", "Google Scholar", "SpringerLink", and "Open Access Journal Search Engine". Overall means all kinds of data including research article, review, short notes, editorial commentary, research articles, books and book chapters, etc., that were published from 1 January 2016 to 30 June 2021. Target pollutants were tested either individually or in mixture with other contaminants.

In the next sections all the data overviewed in the literature since 2016 are summarized according to their chemical class.

3.1. Microplastics, Nanoplastics and Plastic-Derived Chemicals

A great variety of synthetic organic polymers such as polystyrene (PS), polyethylene terephthalate (PET), polymethylmethacrylate (PMMA), polyethylene (PE), polypropylene (PP), polyvinylchloride (PVC), polytetrafluoroethylene (PTFE), and others are known by the term plastics, and are associated with specific applications and consumer products. Furthermore, a wide diversity of plastic-derived chemicals such as bisphenol A (BPA) and di-(2-ethylhexyl) phthalate (DEHP) can be present in coastal waters as well as in the open sea.

Several polymers are currently used world-wide due to their unique properties, including: (i) chemical stability and long durability, (ii) low weight, and (iii) ease to be shaped, transformed, and manufactured. Though there exist advantages regarding the convenience and practicability in their use and numerous applications, their principal drawbacks are that these materials are very resistant to chemical and biological degradation and thus exhibit long persistence into the environment.

Large amounts of plastic waste penetrate sea systems after their direct or indirect release into the marine and estuarine ecosystems, and afterward they are dispersed throughout the global ocean, and hence defined as plastic litter [7,8]. According to the recent

review of Gonçalves and Bebianno (2021) most of the plastic debris found in the marine environment originates from land-based sources [8], while the environmental behavior, distribution, and fate of MPs and NPs are strongly dependent on the affinity and stability of their formed aggregates. In the review work of Ajith et al. (2020), among the most frequently detected polymers in the marine environments low-density polyethylene (LDPE), high-density polyethylene (HDPE), PP, PS, PET, and PVC are included, while also present are several polymers such as acrylic, nylon, polyurethanes, polycarbonate, polylactic acid, and other biodegradable plastics [7].

It has been reported that approximately 8 million tons of plastics are being dumped into the sea annually [9]. The survey of Boucher and Friot (2017) revealed the microplastic debris contribution by certain geographical areas, namely Southeast Asia (15.9%), North America (17.2%), and Africa and Middle East (8.7%) [10].

Even though a precise, accurate and united definition of MPs and NPs has not yet been established in the literature, as scientists are still disputing [11], the majority of the authors have defined MPs as the particles of synthetic polymers with sizes <5 mm or <1000 μm to >0.1 μm or 1 μm to 1 mm [12], while NPs are the pieces of plastics with a size <20 μm or <0.1 μm or <1 μm or <100 nm or <1000 nm [13]. Those materials can be further divided into primary and secondary MPs and NPs. Primary MPs and NPs are the particles that launch into the environmental compartments in their original small size (within the corresponding size scale described above), whilst secondary MPs and NPs are those particles that are formed as a consequence of macro/microplastic degradation of larger plastic materials [8].

Barreto et al. (2015) [14] surveyed the behavior of colloidal gold nanoparticles in different ionic strength media and highlighted the fact that nanoparticles when contained in saltwater are expected to aggregate/agglomerate and consequently, differences in terms of decreased bioavailability with increased concentration due to aggregation must be taken into account.

The toxic effects of MPs and NPs on different marine biota has been demonstrated by numerous researchers during the last 5.5 years, and a rising research interest can be observed in investigating the toxicity of those group of emerging pollutants towards various marine organisms, as illustrated in Figure 3. Based on the found and reviewed data it is shown that a great variety of marine plant and animal species have been employed to evaluate the toxicological effects of MPs, NPs, and plastic-derived chemicals such as bisphenol A (BPA), di-(2-ethylhexyl) phthalate (DEHP), polybrominated diphenyl ethers (PBDEs) and others (Table 1).

Various species of marine bacterium have been exposed to small size polymers of different types and sizes and under different experimental conditions (concentration, duration, etc.). The toxicities of PS-NPs and PS-nano beads (PS-NH_2, 50 nm and PS-beads, 55 nm, respectively) towards the marine bacterium *Halomonas alkaliphila* was investigated by Sun et al. (2018) [15]. The results indicated that in the presence of polymers, particles with size 50 nm at concentrations between 20–320 μg mL^{-1} after 2 h exposure affected the bacterium and resulted in inhibition of growth rate, decreased chlorophyll content, and increased oxidative damage of the exposed microorganisms [15]. Moreover, according to the same study, compared to PS-nano beads, PS-NH_2 induced higher oxidative stress on the exposed bacterial species [15].

Marine bacterium strains *Marinobacter adhearens*, *Oceanobacter kriegii*, *Cobetia marina*, *Marinobacter algicola*, *Pseudoalteromonas carrageenovora*, and *Phaeobacter inhibins* were used by Okshevsky et al. (2020), and the formation of biofilm by the selected marine bacteria when exposed to PS NPs was impacted by concentration and surface functionalization of polymer NPs in a species-specific manner [16]. It was observed that whereas PS-COOH increased the amount of biofilm formed by several species, on the contrary, amidine-functionalized NPs decreased the amount of biofilm of the tested bacteria with the exception of *Oceanobacter kriegii*. In addition, it was suggested that the aggregation dynamics of bacteria and NPs were strongly impacted by the surface properties and concentration of the NPs [16].

Table 1. Selected studies evaluating the toxicity of MPs, NPs and plastic-derived chemicals on marine plant and animal species.

Tested Species	Polymer Type	Main Findings	Reference
Chaetoceros decipiens-lorenzianus (Cosmopolitan diatom)	BPA and DEHP (separately and in mixture)	Slight but significant stimulation of biomass and photosynthetic activity upon short-term exposure (first 48 h) that was followed by a return to control conditions for all treatments at the end of incubation (7 days).	M'Rabet et al., 2021 [17]
Chlorella sp. (Microalgae) and *Artemia salina* (Zooplankton crustaceans)	PS microplastics on nano-TiO_2 (carboxylated, plain, and aminated)	In both species nano-TiO_2 toxicity increased with the addition of plain PS and NH_2-PS and decreased with the addition of COOH-PS. Aqueous exposure to *Artemia salina* was more toxic than dietary exposure. No biomagnification of nano-TiO_2 from *Chlorella* sp. to *Artemia salina* was noted.	Thiagarajan et al., 2021 [18]
Crassostrea gigas (Pacific oyster)	HDPE (20–25 µm, 112 microplastics mL^{-1}, eitheralone or in combination with chlortoluron (herbicide))	MPs exposure induced an increase of micro-closure frequency, and a decrease of valve opening duration. MPs alone and in a cocktail with chlortoluron reduced the shell growth.	Bringer et al., 2021a [19]
Mytilus spp. (Blue mussels, Juvenile)	PVC particles (15, 1500, 15,000, 150,000, 1,500,000 particles/individual/week calibrated in the size range 11–60 µm) and regularly shaped PS beads (15, 1500, 15,000 particles/individual/week, 40 µm)	Effects were seen even at the lowest MP concentration (15 particles/individual/week). At the highest PS dose, clearance rates decreased significantly only after 36 weeks. SOD and MDA concentrations declined as a consequence of exposure to microplastics.	Hamm et al., 2021 [20]
Oryzias melastigma (Marine medaka)	PE and PVC MPs	Growth and reproduction were disrupted after four months of exposure. Severity of the disruptions depends on plastic types.	Cormier et al., 2021 [21]
Brachionus plicatilis (Rotifer) *Nannochloropsis gaditana*, and *Tetraselmis chuii* (Microalgae)	Nanosized PMMA	PMMA-NPLs long-term exposure through food increased rotifers reproduction output. *T. chuii* promoted better reproductive output in exposed organisms than *N. gaditana*.	Venâncio et al., 2021 [22]
Allivibrio fischeri (Marine bacteria)	11 compounds belonging to the group of PET precursors	Three compounds harmful to nematode *Caenorhabditis elegans* only at high concentration. Six compounds classified as toxic and moderately toxic against *Allivibrio fischeri*.	Djapovic et al., 2021 [23]
Tegillarca granosa (Marine clam)	MPs in mixture with a mixture of PAHs standard mix of 16 representative PAHs	Exposure to PAH mixtures and MPs altered haematic parameters of blood clam, resulted in increase of ROS production, lipid peroxidation and DNA damage, reduced haemocyte viability and disrupted key molecular pathways. MPs and PAH mixtures exerted significant synergistic toxic impacts on blood clam.	Sun et al., 2021 [24]
Mytilus galloprovincialis (Marine bivalve)	PET-MFs	PET-MFs (length 50 and 100 µm) affected cellular immune responses in mussels. Short MFs accumulated in lower organs and long MFs in upper organs. AChE activity is sensitive to short MFs, while DNA damage to long MFs at environmentally relevant concentration. Length dependent type of toxicity disappeared at high concentration.	Choi et al., 2021 [25]
Acartia tonsa (Marine copepod)	PE-MPs (particles (1–50 µm)) individual and combined effects of PE-MPs and chlorpyrifos (organophosphate pesticide)	PE-MPs did not cause toxic effects in sub-lethal fitness responses but increased chlorpyrifos toxicity to copepods. Microplastics may act as vectors of environmental pollutants to marine organisms and can represent an indirect pathway of exposure to pollutants in marine organisms.	Bellas et al., 2020 [26]
Dunaliella tertiolecta (Microalgae)	Leachates of different virgin polymers, PP, PE, and PS	An algae inhibition growth ranking (PP > PS > PE) was noted, based upon EC50 values. ROS generated were increased with leachates concentrations with PS exhibiting the highest ROS levels, while a marked genotoxic effect (30%) was found only with PP.	Schiavo et al., 2020 [27]

Table 1. *Cont.*

Tested Species	Polymer Type	Main Findings	Reference
Chlorella pyrenoidosa (Green microalgae) and *Daphnia magna* (Planktonic crustacean)	Iron-oxide-doped microplastics	Amine-modified iron oxide–doped polystyrene microplastics induced greater toxicity to *Chlorella pyrenoidosa* in comparison to carboxyl-modified polystyrene microplastics with/without iron oxide doping.	Zhang et al., 2020 [28]
Skeletonema costatum (Diatom)	Copper nanoparticles with microplastic exposure	The sorption of Cu^{2+} on micro-sized polyvinyl chloride lessened the toxic effects of nano-Cu in microalgae.	Zhu et al., 2020 [29]
Chlorella pyrenoidosa (Microalgae)	Combined effect of PS microplastics and dibutyl phthalate	5.0-µm-sized PS particles (up to 64 mg L^{-1}) induced little effect on the growth of *Chlorella pyrenoidosa*.	Li et al., 2020 [30]
Tetraselmis chuii (Microalgae)	Gold nanoparticles and microplastics mixtures	The mixture containing high concentrations of MPs and gold nanoparticles was more toxic than their individual counterparts.	Davarpanah and Guilhermino, 2019 [31]
Chlorella sp. (Microalgae)	PS microplastics on nano- P25 TiO_2	The presence of plain and aminated PS microplastics (1000 mg L^{-1}) could additively increase the toxic effects of nano-TiO_2 (3, 6, and 9 mg L^{-1}) in comparison to the carboxylated PS microplastics (1000 mg L^{-1}), which antagonistically decreased the toxic effects of nano-TiO_2 after a 72-h incubation.	Thiagarajan et al., 2019a [32]
Chlorella pyrenoidosa (Microalgae)	Combined effect of PS plastics and triphenyltin chloride	The algal surface could adsorb microplastics and disturb the membrane transport and could cause detrimental damage to the membrane structure.	Yi et al., 2019 [33]
Perna viridis (Asian green mussel)	Micro-sized PVC particles (1–50 µm)	Microplastics exposure (at 0, 21.6, 216, and 2160 mg L^{-1} for 91 days) impaired the mussels' physiological performance and increased mussel mortality. The size of the induced effect was dose-dependent.	Rist et al., 2016 [34]

Notes: BPA: bisphenol A; DEHP: di-(2-ethylhexyl) phthalate; HDPE: high-density polyethylene microparticles; MDA: malondialdehyde; MFs: microfibers; PET: polyethylene terephthalate; PE: polyethylene; PMMA: polymethylmethacrylate; PP: polypropylene; PS: polystyrene; PVC: polyvinylchloride; ROS: reactive oxygen species; SOD: superoxide dismutase.

Several marine microalgal species have been utilized for the ecotoxicological evaluation of small-sized particles of plastics, and among the reviewed herein literature the microalgae strains *Dunaliella tertiolecta* (exposed to PS beads of 50 nm at 250 µg mL^{-1} for 72 h [35]; exposed to PS-NH_2 of 50 nm, and PS-COOH of 40 nm for the same time as previous [36]; exposed to leachates of different virgin polymers, PP, PE [27]), *Tetraselmis chuii, Nannochloropsis gaditana, Isochrysis galbana* (exposure to polymethylmethacrylate (PMMA) with size 40 nm, at concentrations 0–304.1 mg L^{-1} for 96 h, [37]), *Rhodomonas baltica* (exposed to PMMA and PMMA-COOH with size 50 nm, at 0.5–100 µg mL^{-1} for 72 h, [38]), and the marine diatoms *Thalassiosira weissflogii* (exposure to PMMA with size 40 nm, at concentration levels 0–293.0 mg L^{-1} for 96 h [37]), and *Chaetoceros neogracile* (exposure to PS-NH_2 with size 50 nm, at 0.05 µg mL^{-1} and 5 µg mL^{-1} for 96 h [39]) are included, among several others.

In general, many published reports have investigated and reported the effects of MPs and NPs on several microalgae and microcrustacean species belonging to these two low trophic levels that are both at the bottom of the food chain of marine environments, as prey and predator, correspondingly. In addition, the combined toxicity of microplastics and various nanomaterials on those marine species has been assessed, such as gold nanoparticles [31] and nano-TiO_2 particles [18,32,40–43]. Furthermore, the toxicity of amine-modified iron oxide–doped polystyrene microplastics and carboxyl-modified polystyrene microplastics has been evaluated [28].

The toxic mechanisms of MPs and NPs affecting the exposed microalgae and microcrustacean species has been elucidated in several cases, and among them growth inhibition [27], effect of photosynthesis by blocking the light transport and access [44],

disturbance of the membrane structure and transport [33], metabolism disorders [27], DNA damage [27], genotoxic effect [27], and oxidative stress [27,44] are included.

According to a recent survey of Hou et al. (2019) that reviewed the scientific literature on toxic effects of TiO_2-NPs on different organisms, the toxicity mechanism on multiple taxa of microorganisms including plants, algae, invertebrates, and vertebrates can be outlined in three features: (i) the generation of reactive oxygen species (ROS) after the penetration of electron-hole pairs; (ii) the formation of NP–cell bonds through electrostatic nature interactions (that are favored by the large surface area of TiO_2-NPs) that cause the destruction of the cell wall structure and lipid peroxidation of the cell membrane; and finally (iii) the connection of TiO_2-NP with the biological macromolecules and intracellular organelles [43].

Overall, the studies regarding the impacts of MPs and NPs on microorganisms at the bottom of the food chain, such as microalgae, rotifers, and polychaetes, have demonstrated particle and species-specific responses [45]. For instance, Venâncio et al. (2019) [37] reported that organisms that have the role of primary and secondary consumers as zooplankton members, such as *Brachionus plicatilis* (rotifers), can be more sensitive to PMMA-NPs (size 40 nm; 96 h; at concentrations 4.7–75.0 mg L^{-1}) exposure than organisms that are producers, such as the microalgae *Tetraselmis chuii* and *Nannochloropsis gaditana* [37]. Manfra et al. (2017) [46] showed that with *Brachionus plicatilis*, after its short exposure (24–48 h) to PS-COOH (size 40 nm) and PS-NH_2 (size 50 nm) at concentration levels that ranged between 0.5 and 50 mg L^{-1}, high mortality due to PS-NH_2 was observed, whereas on the contrary no acute toxicity due to the PS-COOH was illustrated [46]. The results of a survey conducted by Jeong and Choi (2019) [47] revealed that with marine rotifer *Brachionus koreanus*, when exposed at a concentration of 10 μg L^{-1} to two different sizes of PS-NPs (500 and 6000 nm, and 50 nm, respectively), it was suggested that the molecular initiating event was ROS formation [47]. Even though data on the ecotoxicological effects of MPs and NPs on rotifers are scarce [37,46,47], the reviewed literature herein indicates that in general the toxicity that is observed, such as oxidative stress, induced damage to lipid membranes, accumulation, and mortality, is dependent on both type and size of polymers.

Based on the reviewed data within the current study, PS-NH_2 comparatively possess a more toxic effect on echinoderms than PS-COOH, as seen and described above in bacteria, algae and rotifers [8,36,48,49]. For example, it has been reported by Bergami et al. (2019) [49] that PS-NPs affected the innate immune system of the Antarctic sea urchin *Sterechinus neumayeri*, while amino-modified PS-NPs affected signaling pathways of the sea urchin *Paracentrotus lividus* embryos, according to Pinsino et al. (2017)] [48].

The impacts of PS-NPs on the ability of the polychaeta *Hediste diversicolor* were assessed by Silva et al. (2000a and 2000b) [50,51] and the results of their study revealed the effects on burrowing behavior and regenerative capacity [50,51].

Marine crustaceans such as planktonic and benthic organisms are useful and important test organisms used in the bioassays concerning the toxicity and impacts of plastics in marine ecosystems. These organisms possess both the role of primary and secondary consumers and thus are considered as the connectors between the primary producers and the higher level consumers, hence are responsible for the corresponding energetic fluxes (trophic transfers) within the food web. Effects of MPs and NPs on several crustaceans have been assessed, such as brine shrimp *Artemia franciscana* [36,52], nauplii of the acorn barnacle *Amphibalanus amphitrite* [53,54], and Antarctic krill juveniles, *Euphausia superba* [55]. Effects of PS-COOH (40 nm) and PS-NH_2 (50 nm) particles on the expression of two genes, cathepsin L-associated protein (clap) and cathepsin B (cstb), which are connected to the growth of *Artemia franciscana*, were reported after their exposure to 0.5–10 μg mL^{-1} for 24 and 48 h [36]. Moreover, according to the same researchers, the results of the growth inhibition test (72 h) and a long-term sub-lethal test (14 d) revealed that tested pollutants were retained inside the gut lumen and thus had been accumulated. PS-COOH particles were less toxic than PS-NH_2, once again [52]. Accumulation of PS particles was also observed in the case of *Amphibalanus amphitrite* simultaneously with other effects

such as the impact on the organism's swimming speed and mobility inhibition observed by Gambardella et al. (2017) [53]. Similar observations for bioaccumulated particles of polymers were reported for the same crustacean, A. *amphitrite*, after its exposure to PMMA (45 nm; 5–25 μg mL^{-1}; 24 h) [54].

Unquestionably, bivalves have been characterized as excellent sentinel organisms for ecotoxicological evaluations and bioindicators not only due to their wide geographical distribution but also due to their ability to accumulate several chemicals that are present in their ecosystem through their filter-feeding mechanism [8]. Interestingly, in a recently published survey of Hamm et al. (2021) [20], who exposed juvenile *Mytilus* spp. to environmentally realistic doses of irregularly shaped PVC particles (from 15 to 1,500,000 particles/individual/week calibrated in the size range 11–60 μm) and regularly shaped PS beads (from 15 to 15,000 particles/individual/week, 40 μm) over 42 weeks, the negative effects of the tested microplastics on mussel performance (in terms of on clearance rate, byssus production, growth rate, superoxide dismutase activity, malondialdehyde concentrations, and the condition index) emerged late in the experiment and were rather weak [20].

The impacts of the cationic polystyrene nanoparticles (amino-modified PS-NH_2) on early embryo development of Mediterranean mussel, *Mytilus galloprovincialis*, and more specifically the effects on shell formation, were investigated by Balbi et al. (2018). Based on their published results, the studied emerging pollutants were shown to affect gene expression profiles during early embryo development, because decreased mineralization and shell size was observed at a concentration of 0.150 mg L^{-1} (≅EC_{50}) with malformed D-veligers, whereas higher concentrations (in the range of 5–20 mg L^{-1}) resulted in high embryotoxicity/developmental arrest [56].

In the study of González-Fernández et al. (2018) [57] regarding the cellular responses of Pacific oyster (*Crassostrea gigas*), it was reported that in gametes exposed in vitro to PS-NPs, tested NPs (PS-COOH and PS-NH_2, 100 nm; 0.1–100 mg L^{-1}) attached to both oocytes and spermatozoa, and cellular impacts on spermatozoa were observed. Furthermore, PS-COOH exposure generated a dose–response increase in ROS production in spermatozoa, while the higher impact of PS-COOH suggested an influence of particle surface properties [57]. In a more recent investigation conducted by Bringer et al. (2021) [19] on the Pacific oyster, *Crassostrea gigas*, they discovered that the sub-chronic exposure to HDPE MPs alone or in combination with the pesticide chlortoluron significantly affected valve activity and daily growth of the tested bivalve [19].

The presence of MPs and NPs in the gastrointestinal system of several fish species has been exhibited by a number of researchers, the majority of which seems to agree with the recommendation that the detected MPs are either ingested accidentally (because fishes are habituated to ingest various indigestible particles such as sand, fish scales, and shells of smaller invertebrates) or have been transferred through the food chain from lower to higher trophic levels [7,58]. The findings of the present review revealed that most of the available literature data have focused on the effects of MPs and NPs on freshwater fish species [59–64], whereas the corresponding research regarding the impacts on marine fish species are fewer [45,65–69]. Common bluegill (*Lepomis macrochirus*) [65], Atlantic salmon [65], European seabass (*Dicentrarchus labrax*) [66,69], rainbow trout (*Oncorhynchus mykiss*) [67], gilthead seabream (*Sparus aurata*) [45,69], and marine fish *Dicentrarchus labrax* [68] are some of the fish species on which the potentially toxic effects of exposure to several and different types and sizes of MPs and NPs has been scrutinized.

Based on the findings of Mallik et al. (2021) [9] who summarized the scientific data on ecotoxicological and physiological risks of MPs on fish and their possible sources, routes, bioavailability, trophic transfer, and consequences, it was concluded that the ingested MPs could cause severe health implications, including improper gill functioning, immunosuppression, reduced feeding intensity and compromised reproducibility. Several review studies have also been conducted in the same period to investigate the mobility and bioaccumulation of chemical stable MPs and NPs into aquatic biota via the food chain from

primary producers to top predators [3,70–77]. According to the aforementioned review of Mallik et al. (2021), the ingestion of plastic debris by fishes can either directly cause lethal effects and mortality (due to choking and internal injuries) or sub-lethal damages via intestinal alterations and injuries that may reduce nutrient intake. Disruption of various metabolic processes, such as fat metabolism, immune system, and hepatic stress, induced different physiological changes, such as behavioral changes and reduced ability to sense predators, are also some possible consequences of direct or indirect ingestion of MPs and NPs in the gastrointestinal tract of fish [9].

An important indicator that has been recognized as adequate in assessing the toxic impacts of small size plastic pollutants in exposed fish on a molecular scale is fish cell lines and the infection of them with the pancreatic necrosis virus [65–67]. The use of this tool enables scientists to avoid the employment of animals in their experimental sections as proposed by the Directive 2010/63 EU of the European Union [8]. For instance, Almeida et al. (2019) [69] surveyed how PS-NPs could alter the cytotoxicity of human pharmaceuticals on marine fish cell lines of the sea bream *Sparus aurata* and the seabass *Dicentrarchus labrax*, and reported that 100 nm PS plastics may alter oxidative status and biotransformation of the exposed species. Specifically, a slight decrease (25%) in the viability of cell lines of the *S. aurata* and the *D. labrax* at lowest concentrations was observed, starting at 0.001 up to 10 mg L^{-1}, to assess effects on viability and activity of catalase and glutathione *S*-transferases [69].

Brandts et al. (2021) reported that short-term exposure of the seabream *S. aurata* to PMMA (size 45 nm; concentration range 0–10 mg mL^{-1}; 24 and 96 h) resulted in upregulation of the mRNA levels of essential lipid metabolism-related genes that controlled the increase in plasma cholesterol and triglycerides [45]. The increase in abundance of mRNA transcript, as well as the impairment of the fish's immune system, was also described by the same authors [68] in their previous study regarding the seabass *D. labrax* after their exposure to the same NP and size (PMMA; 45 nm; 0–20 mg/L; 96 h). PS disturbed the pentose phosphate pathway and nucleotide metabolism in the liver of the marine medaka (*Oryzias melastigmas*), suppressed hepatic organic acids in the tricarboxylic acid cycle and glycolysis and most monosaccharides and amino acids in the liver, and induced accumulation of hepatic fatty acids, fatty acid methyl, and ethyl esters, while the PS size affected hepatic metabolism and PS accumulation [78]. The conclusions of the study conducted by Gonçalves and Bebianno (2021) [8] have shown that small particles of synthetic polymers of several types and sizes can disrupt the immune system of fish, induce oxidative stress, compromise lipid metabolism and cause cell viability to decline.

In a recent study, Ajith et al. (2020) [7] revealed that even though microplastics are undeniably one of the most crucial and urgent environmental threats that are detected in almost all the marine habitats and biota of the world, only a low number of countries have performed research regarding their distribution in the marine environment (44 countries, equal to 22.9% of the overall 192 countries of the world). The same authors observed that the research investigating their impacts on organisms have mostly targeted fish (38%), while on the contrary surveys on other highly affected organisms such as turtles (1%) were not well documented [7].

Moreover, it has been well documented in the relevant bibliography that various organic and inorganic compounds such as PCBs and PAHs, which are among the most reported adsorbates found in MPs [79], as well as pharmaceuticals [80,81], pesticides [26,82], heavy metals [83] and other contaminants, are widely present in the sea environment [84]. The affinity of coexisting pollutants towards MPs and NPs is dependent on several different parameters, such as the type of both pollutant and polymer, the size of plastic pieces (MPs or NPs), the type and energy of chemical intermolecular forces of interaction (van der Waals, hydrogen bonding, π–π interaction, etc.), and the gradual changes in their chemical bonds over time (ageing) [84]. Usually, after their ingestion, the contaminants adsorbed onto plastics are desorbed in the intestine of organisms (especially benthic invertebrates, fish,

deep ocean biota, and larger mammals) and their translocation follows to the circulatory system, tissues, intestinal epithelia, liver, and other organs.

The combined effects of MPs- or NPs-pollutants complexes has been assessed in a number of studies [26,85–95]. A recent study by Bellas et al. (2020) [26] revealed that even though PE-MPs did not induce any toxic impact in sub-lethal fitness responses (such as fecundity, feeding, and egg viability) of exposed *Acartia tonsa* individuals, the tested MPs increased the toxicity of the organophosphorus pesticide chlorpyrifos on the widely distributed calanoid copepods in planktonic communities [26]. Similarly, synergistic impacts of MPs and some PAHs have been reported in the bibliography on some marine organisms [91–95], among which Mediterranean mussels *Mytilus galloprovincialis* [91,95] and the blue mussel *Mytilus edulis* [93] are included. However, more research in this direction in the future must be performed with more realistic scenarios of more compounds simultaneously present in the tested cocktails of chemicals.

3.2. Pharmaceuticals

Pharmaceuticals, also identified as drugs or medicines, are chemical substances that are used for the treatment, diagnosis, or prevention of a specific disease. Among these chemical substances several classes of human and veterinary pharmaceuticals are included, such as antibiotics, anti-inflammatory drugs, antidepressants, antineoplastic or anticancer drugs or immunomodulating agents, and several other different groups that are discovered, developed, produced, and marketed to patients in order to cure, vaccinate or alleviate the symptoms of a wide variety of human and animal illnesses. During the past years and up to today, remarkable increasing research and development in the processes of discovering and designing new pharmaceuticals has been achieved, and has resulted in a wide range of medicines utilized all over the world.

For instance, more than 250 registered antibiotic drugs, subdivided mainly into six different classes, including macrolide, β-lactam, tetracyclines, fluoroquinolones, sulfonamide, and diaminopyrimidine, are currently available in the global market of pharmaceuticals. As a consequence, residues of pharmaceuticals can be found and detected in several water bodies around the world. Due to their increasing consumption, combined with their incomplete removal in wastewater treatment plants, their detected concentrations in the aquatic environment can range from ng L^{-1} to μg L^{-1} [96]. According to the relevant data, the occurrence and spatial distribution of several pharmaceuticals and related metabolites have been observed in a variety of aqueous environmental samples of wastewater, surface water, groundwater, drinking water, and transitional systems such as estuaries and coastal systems (offshore seawater) [4,5,97,98].

The effects induced by pharmaceuticals on non-target aquatic organisms are dependent on many factors, among which the sensitivity of the exposed organism, the type of pharmaceutical, the exposure concentration, and the duration of exposure are the most important that are reported in the reviewed literature. In general, factors related to experimental designs and biological materials are applied to determine the results obtained after an ecotoxicological assessment experiment.

Some of the studies reviewed herein were selected to be presented in summary regarding the experimental information (tested pharmaceutical and target marine organism) and the main findings and highlights are reported in Table 2.

Several recent studies during the last 5.5 years have shown the impacts of pharmaceuticals on marine organisms such as fish species [99–101] (*Argyrosomus regius* [99], *Sparus aurata* [100], *Salmo trutta* [101] among others), algae (*Chlorella pyrenoidosa* and *Anabaena cylindrica*, [102]), and invertebrates such as bivalves [96,98,103–115] (clams *Ruditapes philippinarum* [98,103,104,107,111,112] and *Ruditapes decussatus* [112], European mussel *Mytilus galloprovincialis* [96,103,105,106,108,112–115], blue mussels *Mytilus edulis* [109], thick shell mussel *Mytilus coruscus* [116], and peppery furrow shell *Scrobicularia plana* [110], among others), polychaetes [117–121] (*Diopatra neapolitana* [117,118], *Arenicola marina* [118], and

Nereis diversicolor [119–121], among others), crustaceans (e.g., *Daphnia magna* [122]), and echinoderms (such as sea urchin *Paracentrotus lividus* [123]).

Table 2. Selected studies evaluating the toxicity of pharmaceuticals on marine plant and animal species.

Pharmaceuticals	Tested Species	Main Findings	Reference
Amoxicillin (Antibiotic)	*Ruditapes philippinarum* (Bivalve, clam)	SOD and CAT activities, as well as the LPO levels and PCC were measured in bivalves exposed to 100, 200 and 400 μg L^{-1} for 1, 3 and 7 days. The results obtained demonstrated that tested antibiotic slightly affected biomarker responses of mollusks.	Matozzo et al., 2016a [103]
		The bivalves were exposed to 100, 200 and 400 mg L^{-1} for 1, 3 and 7 days, and the effects on the THC, the diameter and volume of the haemocytes, haemocyte proliferation, LDH activity in cell-free haemolymph, the haemolymph pH, and the formation of micronuclei were evaluated.	Matozzo et al., 2016b [104]
	Mytilus galloprovincialis (Bivalve, mussel)	SOD and CAT activities, as well as the LPO levels and PCC were measured in bivalves exposed to 100, 200 and 400 μg L^{-1} for 1, 3 and 7 days. The results obtained demonstrated that tested antibiotic slightly affected biomarker responses of mollusks. Antibiotic slightly affected the haemocyte parameters of bivalves.	Matozzo et al., 2016a [103]
		SOD and CAT activities, as well as the LPO levels and PCC were measured in bivalves exposed to 100, 200 and 400 μg L^{-1} for 1, 3 and 7 days. The results obtained demonstrated that tested antibiotic slightly affected biomarker responses of mollusks. Antibiotic slightly affected slightly the haemocyte parameters of bivalves	Matozzo et al., 2016b [104]
Cetirizime (antihistamine)	*Mytilus galloprovincialis* (Bivalve, mussel)	Induced toxic effects leading to oxidative stress. Mussels maintained their metabolic activity up to the highest concentration (12.0 μg L^{-1}). Enhanced activity of antioxidant enzymes SOD and CAT. Inhibition of the activity of biotransformation enzymes (GSTs). Defense mechanisms were unable to prevent LPO that increased along exposure gradient.	Teixeira et al., 2017 [96]
Cisplatin (antineoplastic, anticancer)	*Mytilus galloprovincialis* (Bivalve, mussel)	Exposure to drug at levels up to 100 ng L^{-1} imbalanced the activity of defense enzymes in gills and digestive gland. Neurotoxicity, oxidative and DNA damage were noticed.	Trombini et al., 2016 [105]
	Nereis diversicolor (Polychaete)	After exposure for 14 days at levels 0.1–100 ng L^{-1} induced behavioral impairments and neurotoxicity was observed. Oxidative stress and lipid peroxidation were observed after cytotoxic exposure. DNA damage was not detected in coelomocytes of polychaetes exposed.	Fonseca et al., 2017 [119]
	Nereis diversicolor (Polychaete)	Marine polychaetes exposed to mixtures of anticancer drugs (cyclophosphamide and tamoxifen), at environmental levels (10–100 ng L^{-1}) for 14 days. Toxicity of mixtures did not follow a dose–response pattern. Oxidative damage and genotoxicity occurred at the lowest levels of drug mixtures. Toxicity of mixtures disregarded the effects of single compounds.	da Fonseca et al., 2019 [121]
Cyclophosphamide (antineoplastic, anticancer)	*Nereis diversicolor* (Polychaete)	Exposure at trace levels (concentration range 10–1000 ng L^{-1} for 14 days) in seawater. Burrowing behavior showed a non-monotonic profile over increasing cyclophosphamide levels. Oxidative stress was observed at higher cyclophosphamide concentrations. Genotoxicity was detected as a result of prodrug activation. *N. diversicolor* showed to metabolize the drug according to its mode of action.	Fonseca et al., 2018 [120]
	Nereis diversicolor (Polychaete)	Marine polychaetes exposed to mixtures of anticancer drugs (cyclophosphamide and tamoxifen), at environmental levels (10–100 ng L^{-1}) for 14 days. Toxicity of mixtures did not follow a dose–response pattern. Oxidative damage and genotoxicity occurred at the lowest levels of drug mixtures. Toxicity of mixtures disregarded the effects of single compounds.	da Fonseca et al., 2019 [121]

Table 2. *Cont.*

Pharmaceuticals	Tested Species	Main Findings	Reference
	Mytilus galloprovincialis (Bivalve, mussel)	Assessment of in vivo and ex vivo toxicity at levels up to 1000 ng L^{-1} for 14 days. In vivo exposure to cyclophosphamide provoked oxidative stress and oxidative damage in tissues. DNA damage reported in mussels exposed over 14 days to drug. Cytotoxicity registered in mussels hemocytes. Likely metabolic activation of tested pharmaceutical in mussels and prompt of its mode of action.	Fernandes et al., 2020 [8]
Erythromycin (antibiotic)	*Sparus aurata* (Fish, gilthead seabream)	Caused undesirable effects in several metabolic pathways of fish. Induced slight pro-oxidative and genotoxic effects. Detoxification responses, energetic imbalance and neurotoxicity were not observed.	Rodrigues et al., 2019 [100]
	Mytilus edulis (Bivalve, blue mussels)	GT and CAT enzymes were induced significantly. Metabolic balances were disturbed under incredibly high erythromycin concentrations. Osmolality, energy, nerve and amino acid metabolism were affected.	Liang et al., 2020 [109]
Carbamazepine (antiepileptic)	*Ruditapes philippinarum* (Bivalve clam)	Limited impacts of drugs at control temperature and warming in clams. No influence of warming on drug uptake and bioconcentration factor in clams. Higher oxidative stress in contaminated clams at control temperature than warming. Impacts of drugs acting together were lower than impacts of single exposures.	Almeida et al., 2021 [98]
	Scrobicularia plana (Bivalve mollusk)	Clams developed mechanisms to prevent oxidative damages when under pH 7.1. The toxicity increased under sea-water acidification conditions.	Freitas et al., 2016 [110]
	Diopatra neapolitana (Polychaete)	Under environmentally relevant concentrations (exposure at concentrations 0–9 µg L^{-1} for 28 d), carbamazepine induced higher impacts on regenerative capacity than caffeine in terms of body width regenerated and number of new segments. With the increase of drug concentrations organisms regenerated less new segments and took longer to completely regenerate.	Pires et al., 2016 [117]
Caffeine (stimulator of the central nervous system)	*Diopatra neapolitana* (Polychaete)	Under environmentally relevant concentrations (exposure at concentrations 0–18 µg L^{-1} for 28 d), carbamazepine induced lower impacts on regenerative capacity than carbamazepine in terms of body width regenerated and number of new segments. With the increase of drug concentrations organisms regenerated less new segments and took longer to completely regenerate.	Pires et al., 2016 [118]
	Ruditapes philippinarum (Bivalve, clam)	After exposure for 28 days to caffeine (0.5, 3.0 and 18.0 µg L^{-1}) increase in clam's antioxidant and biotransformation enzymes activity was observed. Clams were not able to prevent cells from lipid peroxidation. With the increase of caffeine concentrations, clams increased their metabolic activity and reduced their energy reserves.	Cruz et al., 2016 [111]
Diclofenac (nonsteroidal anti-inflammatory)	*Ruditapes philippinarum and Ruditapes decussatus* (Bivalve, clams)	Under actual conditions, *R. philippinarum* individuals exposed to the drug presented enhanced antioxidant activities and reduced their respiration rate compared with non-contaminated clams. Although tested clams may use different strategies to prevent diclofenac damage, both clam species showed under low pH and high temperature limited oxidative stress impacts in line with a lower diclofenac bioaccumulation.	Costa et al., 2020 [112]
Irbesartan (Angiotensin II receptor blocker, anti-hypertensive)	*Salmo trutta* (Sea trout)	Irbesartan was not bioconcentrated in tissues above detection limit.	McCallum et al., 2019 [101]
Sulfamethoxazole (sulfonamide antibiotic)	*Mytilus galloprovincialis* (Bivalve, mussel)	Exposure concentration and time dependent sulfomethoxazole accumulation presented in mussels. Antioxidant defense was initiated in vital tissues of exposed marine mussels. Gill was more sensitive under the antibiotic induced stresses compared to digestive gland. Gene expression was more sensitive than responses at protein level. Expression of GSTs gene revealed its potential role in the metabolism of pharmaceutical and ROS elimination.	Chen et al., 2021 [113]

Table 2. *Cont.*

Pharmaceuticals	Tested Species	Main Findings	Reference
Temazepam (Benzodiazepine, Anxiolytic)	*Salmo trutta* (Sea trout)	Temazepam exposure reduced migration speed at the start of migration.	McCallum et al., 2019 [101]
Tamoxifen (antineoplastic, anticancer)	*Nereis diversicolor* (Polychaete)	Marine polychaetes exposed to mixtures of anticancer drugs (cyclophosphamide and tamoxifen), at environmental levels (10–100 ng L^{-1}) for 14 d. Toxicity of mixtures did not follow a dose–response pattern. Oxidative damage and genotoxicity occurred at the lowest levels of drug mixtures. Toxicity of mixtures disregarded the effects of single compounds.	da Fonseca et al., 2019 [121]
Venlafaxine (antidepressant)	*Argyrosomus regius* (Juvenile fish)	The pharmaceutical could be up-taken by fish through both water and diet. Both warming and acidification decreased its uptake in liver, while uptake in brain was favored under warming conditions. Its elimination in liver was impaired by warming and acidification.	Maulvault et al., 2018 [99]

Notes: CAT: catalase; GSTs: glutathione S-transferases; GT: glutathione transferase; LDH: lactate dehydrogenase; LPO: lipid peroxidation; PCC: protein carbonyl content; SOD: superoxide dismutase; THC: total haemocyte count.

According to the gathered data in the current review, it is observed that most of the research has been devoted to assessing the impacts and threats of pharmaceuticals on marine bivalves that are in classes of mollusks that have not only ecological value but socio-economic benefits as well, as edible species [98]. Thus, several species of marine mussels and clams have been studied within the conducted research in order to evaluate the interactive effects of pharmaceutical products. Among the large variety of tested species *Mytilus galloprovincialis*, *Mytilus edulis*, *Mytilus coruscus*, *Ruditapes philippinarum*, *Ruditapes decussatus*, *Scrobicularia plana* and several others are included [96,98,103–115,124–126].

Based on the published results of the relative studies, within the wide list of the reported effects triggered by pharmaceuticals on marine bivalves, alterations related to organisms' oxidative status such as the induction of antioxidant and biotransformation enzyme activities [96,103,104,109], and the occurrence of cellular damages are encompassed. More specifically, individual and sub-individual impacts have been induced and observed by the authors regarding tissue, cellular and molecular levels of biological organization [8]. Lipid peroxidation of cellular membranes of marine mussel *Mytillus galloprovincialis* was observed by Capolupo et al. (2016) after its exposure to caffeine [106], and to marine clams *Ruditapes decussatus* and *Ruditapes philippinarum* by Aguirre-Martínez et al. (2016) after 14-day exposure to caffeine, ibuprofen, carbamazepine, and novobiocin (0.1, 1, 5, 10, 15, and 50 μg L^{-1}) [107]. Induced changes have been observed in oxidative stress-related enzymatic activities, including catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), and glutathione-S-transferase in mussels' tissues after their exposure to a broad spectrum of pharmaceuticals [96,103,104,109].

It is worth noticing that according to a recent study conducted by Costa et al. (2020) [112] investigating the effects of climate change-related factors (temperature and ocean pH) on two clam species to diclofenac (a non-steroidal anti-inflammatory drug), the results showed that both tested species (*Ruditapes philippinarum* and *Ruditapes decussatus*) displayed particular mechanisms to face stress related to warming and ocean acidification (20 °C, pH 7.7; control: 17 °C, pH 8.1). However, the predicted climate change related to warming and ocean acidification (20 °C, pH 7.7; control: 17 °C, pH 8.1) may not enhance the effects of diclofenac in studied clams in a species-dependent manner [112]. This observation is in accordance with the acquired results of a more recent study conducted by Almeida et al. (2021) [98] investigating the combined impacts of ocean warming and antiepileptic and antihistaminic pharmaceuticals (carbamazepine and cetirizine) in the edible marine clam *Ruditapes philippinarum*. Published data highlighted that ocean warming can activate the defense mechanisms of the tested bivalves and reduce their metabolic capacity (lower lipid peroxidation and protein carbonylation levels, higher reduced to oxidized glutathione ratio), especially when both drugs were combined [98].

On the contrary, fewer data exist in the scientific literature regarding the ecological risk of pharmaceuticals to fish species [99–101]. Despite their scarcity, ecotoxicological studies have revealed various biochemical disturbances in fish exposed to human and veterinary drugs (e.g., induced catalytic activity of cytochrome P450), such as oxidative stress, genotoxicity, and neurotoxicity [99–101].

Furthermore, findings of the current review showed that when compared to other classes of pharmaceuticals, the antibiotics have received the most attention up to date, especially if the comparison is done with the anticancer or antineoplastic group of pharmaceuticals, for which a limited amount of information exists [127].

Moreover, in studies conducted with marine and estuarine species, few have demonstrated that temperature rise and ocean acidification scenario will exert changes from the molecular level to ecosystem functioning [98,112,124] and might change the marine organisms' sensitivity to drugs or alter pharmaceuticals' toxicity. For example, in a study by Almeida et al. (2018) evaluating the chronic toxicity of carbamazepine (1 mg L^{-1}) and cetirizine (0.6 mg L^{-1}) on the clam *Ruditapes philippinarum*, for 28 days under control and low pH conditions (pH 7.8 and 7.5, respectively) the transcription of several genes related to neurotransmission, immunity, and biomineralization was revealed by low pH values [124]. More studies should investigate the combined effects of both pharmaceutical drugs and climate-related changes as stressors on marine invertebrates.

3.3. PAHs and PCBs

PAHs, also known as polyaromatic hydrocarbons, are chemical compounds that consist of two or more aromatic rings fused in linear, angular, or clustered arrangements, and are a group of unsaturated organic substances that exhibit high values of molecular weights and low water solubility. Their occurrence in the ocean and marine ecosystems is attributed to both anthropogenic sources (pyrogenic and petrogenic PAHs) as much as to natural sources from oil regeneration processes [128].

Petroleum hydrocarbons pollution is the most common culprit of marine pollution due to leakage from oil refineries or petrochemical factories, accidental spillage from tankers, or/and through atmospheric fallout or waterway-transport from the land, leading to a streak of negative effects for the marine environment. Petroleum is a complex mixture that consists of several different organic substances, among which PAHs, monoaromatic hydrocarbons, aliphatic hydrocarbons, and naphthenic acids are included [129–132].

Based on their molecular weight values, PAHs can be divided into two major categories: (i) those that are composed of less than four aromatic rings (two or three fused benzene rings), such as phenanthrene, naphthalene, fluorene, acenaphthene, and acenaphthylene, which are known as low molecular weight (LMW) PAHs and are more water-soluble; and (ii) those with four or more fused benzene rings, such as chrysene, pyrene, benzo[*a*]pyrene, dibenz[*a*,*h*]anthracene and several others, which are referred to as high molecular weight (HMW) PAHs and which are generally more hydrophobic substances (as they have higher values of the logarithmic form of octanol-water partition constants (log K_{ow}) than LMW PAHs and thus are more readily distributed into organic matter, higher sorption tendency onto organic particles compared to LMW PAHs, lower vapor pressures and Henry's constants). Consequently, a wide variety of benthic organisms can potentially be exposed to PAHs compounds either by being dissolved in the overlying water or alternatively diluted in pore water, or by direct contact with the sea bottom where they are adsorbed.

Overall, this group of POPs is considered as chemical stable compounds with great environmental persistence. Because of their potentially negative ecological health effects, human toxicity, and carcinogenicity, a list of 16 specific PAHs have been prioritized by the U.S. Environmental Protection Agency (USEPA) that are regulated in aquatic and terrestrial ecosystems. Maximum contaminant levels have been established for them in drinking water, whereas according to the relevant toxicological data benzo[*a*]pyrene is considered

to have the highest cancer risk, and furthermore, 7 of these 16 PAHs may cause cancer in humans.

In Table 3 some selected studies reviewed herein are presented in summary regarding the experimental information (tested PAHs and target marine organism) and the main findings and highlights are shown.

Table 3. Selected studies evaluating the toxicity of PAHs on marine plant and animal species.

PAH (s)	Tested Species	Main Findings	Reference
1-Phenylpyrene, Dibenz[*a*,*c*]anthracene, Picene, Indeno [*1*,*2*,*3-c*,*d*]pyrene, Dibenz[*a*,*h*]anthracene, Benzo[*g*,*h*,*i*]perylene, 10-Methylbenzo[*a*]pyrene, 4,5-Dihydrobenzo[*a*]pyrene, 13 H-Dibenzo[*a*,*h*]fluorene, 9 H-Cyclopenta[*a*]pyrene, Perylene, Benzo[*b*]fluoranthene, Benzo[*k*]fluoranthene, Benzo[*a*]pyrene	*Dunaliella tertiolecta*, *Isochrysis galbana*, and *Phaeodactylum tricornutum* (Marine microalgae)	Inhibitions of microalgal growth were observed for fractions of aromatics with log K_{OW} 5–6. Esterase activity was more sensitive, followed by cell membrane integrity and Chl-*a*. 1-Phenylpyrene, dibenz[*a*,*c*]anthracene, and picene were found to be causative agents.	An et al., 2021 [130]
Anthracene, Fluorene, Benzo[*a*]anthracene, Benzo[*a*]pyrene, Benzo[*b*]fluoranthene, Benzo[*g*,*h*,*i*]perylene, Benzo[*k*]fluoranthene, Chrysene, Fluoranthene, Indeno [*1*,*2*,*3-c*,*d*]pyrene, Naphthalene, Phenanthrene, Pyrene, Acenaphthylene, Dibenzo[*a*,*h*]anthracene	*Pseudo-nitzschia hasleana* and *Pseudo-nitzschia mannii* (Diatoms)	Dose-dependent effects on biomass and physiologic endpoints were reported. PAH mixtures induced an increase in cell biovolume, with a greater increase for *P. mannii*. Bioaccumulation and biodegradation of PAHs were reported in *P. mannii* and *P. hasleana* cultures.	Melliti Ben Garali et al., 2021 [131]
1-Methylnaphthalene	*Acropora cervicornis*, *Solenastrea bournoni*, *Stephanocoenia intersepta*, *Siderastrea siderea*, and *Porites astreoides* (Anthozoa, Staghorn coral, scleractinian coral)	The relative sensitivity was assessed with 48-h assays based on physical coral condition, mortality, and photosynthetic efficiency. The threatened staghorn coral *Acropora cervicornis* was found to be the most sensitive. Overall, the acute and subacute endpoints indicated that the tested coral species were comparatively more resilient to hydrocarbon exposure than other marine species.	Renegar et al., 2021 [133]
Benzo[*a*]anthracene Phenanthrene	*Aliivibrio fischeri* (also called *Vibrio fischeri*) (Marine bacteria)	Among other POPs, PAHs showed significant association to the observed bacterial inhibition ($r = 0.28$, $p < 0.05$).	Hwang et al., 2021 [134]
Benzo[*a*]pyrene Phenanthrene 3-Methyl phenanthrene Retene/7-isopropyl-1-methyl phenanthreneAnthracene 2-Methyl anthracene	*Artemia parthenogenetica* (nauplii < 24 h) (Brine shrimp, aquatic crustaceans)	*Artemia* nauplii showed sensitivity differences to six selected PAHs. Survival, behavior, and growth can be affected by all PAHs except Anthracene. Non-polar narcotic mode of action was confirmed not limited to phenanthrene. Body length was proposed as both growth and development indicators for PAH toxicity.	Cong et al., 2021 [135]
A mixture of PAHs (standard mix of 16 representative PAHs*) and MPs	*Tegillarca granosa* (Marine clam)	Exposure to PAH mixtures and MPs altered haematic parameters of blood clam, resulted in increase of ROS production, lipid peroxidation and DNA damage, reduced haemocyte viability and disrupted key molecular pathways.MPs and PAH mixtures exerted significant synergistic toxic impacts on blood clam.	Sun et al., 2021 [24]

Table 3. *Cont.*

PAH (s)	Tested Species	Main Findings	Reference
Benzo[*a*]pyrene	*Chlamys farreri* (Marine bivalve, scallops)	Tested PAH reduced fertility in mature scallops. Gonadal mitochondria and microsome were more vulnerable to lipid peroxidation and protein carbonylation induced by PAH compound. Tested species was more susceptible to DNA damage than ovary under toxicant exposure.	Yang et al., 2021 [136]
Pyrene, Fluoranthene, Fluorene, Acenaphthene, Acenaphthylene, Anthracene, Chrysene, Dibenzothiophene, Methyl-dibenzothiophene, 2/3-Methyl-dibenzothiophene, 4-Methyl-dibenzothiophene, Dimethyl-dibenzothiophene, Trimethyl-dibenzothiophene, Phenanthrene, Methyl-phenanthrene, Dimethyl-phenanthrene, Trimethyl-phenanthrene, Naphthalene, Dimethyl-naphthalene, Trimethyl-naphthalene, Benzo[*a*]anthracene, Benzo(*a*)pyrene, Benzo[*b*]fluoranthene, Benzo[*g,h,i*]pyrene, Benzo[*k*]fluoranthene, Dibenzo[*a,h*]anthracene, Indeno[*c,d*]pyrene, Toluene, Xylene, 1,4-Xylene, 1,2-Xylene, Benzene, Hexochlorobenzene, Ethyl-benzene	*Calanus helgolandicus* (Planktonic copepod)	Significantly elevated mortality rates and impaired molting already in the lowest tested concentrations of each effluent: 0.04 and 0.1%, closed-loop effluents and 1% open-loop effluent, corresponding to total hydrocarbon concentrations of 2.8, 2.0, and 3.8 μg L^{-1}, respectively. None of the individual PAHs analyzed in the effluents occurred in concentrations which could explain the high toxicity.	Thor et al., 2021 [137]
Phenanthrene (alone and in mixture with PS-MPs)	*Oryzias melastigma* (Marine medaka)	The presence of MPs at 20 and 200 μg L^{-1} did not alter the toxicity of phenanthrene (50 μg L^{-1}). Combined exposure to 2 μg L^{-1} MPs and Phe increased the hatchability by 25.8%, decreased malformation and mortality rates, and restored phenanthrene-induced abnormal expressions of cardiac development-related genes	Li et al., 2020 [30]
Benzo[*a*]pyrene (alone and in combination with PS-MPs)	*Tegillarca granosa* (Marine bivalve)	Evident immunotoxicity, as indicated by alterations of haemocyte count, blood cell composition, phagocytic activity, intracellular content of ROS, concentration of Ca^{2+} and lysozyme, and lysozyme activity, was revealed for both microplastics and tested PAH. The toxicity of POPs was generally aggravated by smaller microplastics (500 nm) and mitigated by larger ones (30 mm).	Tang et al., 2020 [92]
Fluoranthene (alone and in mixture with PE or PHB)	*Mytilus galloprovincialis* (Blue mussels)	Activities of SOD, CAT, GPx, GST, and GR were found to be significantly susceptible to fluoranthene and plastics in both tissues. In co-exposure and incubation treatments, biochemical responses were generally comparable with those exerted by PE-MPs or PHB-MPs only, suggesting an apparent absence of combined effects of microplastics with the pollutant.	Magara et al., 2019 [93]

Table 3. *Cont.*

PAH (s)	Tested Species	Main Findings	Reference
Benzo[*a*]pyrene	*Mytilus galloprovincialis* (Blue mussels)	Smaller MPs were able to transfer higher amounts of tested PAH to mussels than larger MPs. Bioaccumulation of benzo[a]pyrene and most biomarkers showed a time dependent response pattern. Large MPs were found mostly in stomach contents and also within epithelial cells of digestive system. Increased effects of MPs-benzo[a]pyrene with respect to MPs alone in hemocyte viability and catalase activity and in digestive gland structure. Effects dependent on MP size were observed on DNA damage and cell type composition of digestive tubules.	González-Soto et al., 2019 [91]
1,4,6,7-Tetramethylnaphthalene, 1-Methylnaphthalene, 2,3,5-Trimethylnaphthalene, 2,3,6-Trimethylnaphthalene, 2,6-Dimethylnaphthalene, 2-Methylanthracene, 2-Methylnaphthalene, Acenaphthene, Acenaphthylene, Anthracene, Benz[*a*]anthracene, Benzo[*a*]pyrene, Benzo[*b*]fluoranthene, Benzo[*e*]pyrene, Benzo[*j*,*k*]fluoranthenes, Biphenyl, C1-Benzo[*a*]anthracenes/chrysenes, C1-Fluoranthenes/pyrenes, C2 Phenanthrenes/anthracenes, C2-Benzo[*a*]anthracenes/chrysenes, C2-Biphenyls, C2-Dibenzothiophenes, C2-Fluoranthenes/pyrenes, C2-Fluorenes, C3-Dibenzothiophenes, C3-Fluoranthenes/pyrenes, C3-Fluorenes, C3-Naphthalenes, C3-Phenanthrenes/anthracenes, C4-Dibenzothiophenes, C4-Naphthalenes, C4-Phenanthrenes/anthracenes, Chrysene, Dibenz[*a*,*h*]anthracene, Dibenzothiophene, Fluoranthene, Fluorene, Indeno[*1*,*2*,*3*-c,d]pyrene, Naphthalene, Perylene, Phenanthrene, Pyrene	Sperm whale skin cells	The water accommodated fraction (WAF) of Alaskan oil was not cytotoxic to sperm whale skin cells though it did induce chromosome damage; S9-mediated metabolism did not affect the cytotoxicity of WAF but did increase the levels of chromosome damage. Chemically enhanced water accommodated fraction of Alaskan (CEWAF) oil was more cytotoxic and genotoxic than the WAF; S9-mediated metabolism increased both cytotoxicity and genotoxicity of CEWAF.	Wise et al., 2018 [138]
Naphthalene, Acenaphthylene, Acenaphthene, Fluorene, Phenanthrene, Anthracene, Fluoranthene, Pyrene, Chrysene, Benzo[*a*]anthracene, Benzo[*b*]fluoranthene, Benzo[*k*]fluoranthene, Benzo[*a*]pyrene, Dibenzo[*a*,*h*]anthracene, Benzo[*g*,*h*,*i*]perylene, Indeno[*1*,*2*,*3*-*c*,*d*]pyrene	*Portunus trituberculatus* (Crab)	Genotoxicity, oxidative stress and reproductive toxicity were observed.	Pan et al., 2017 [129]

Table 3. *Cont.*

PAH (s)	Tested Species	Main Findings	Reference
Naphthalene, Acenaphtene, Fluorene, Phenanthrene, Anthracene, Fluoranthene, Pyrene, Benzo[*a*]anthracene, Chrysene, Benzo[*b*]fluoranthene, Benzo[*k*]fluoranthene, Benzo[*a*]pyrene, Dibenzo[*a*,*h*]antracene, Benzo[*g*,*h*,*i*]perylene	*Dunaliella tertiolecta* (Green microalga), *Amphibalanus amphitrite*, *Artemia salina*, *Corophium insidiosum*, *Brachionus plicatilis* (Rotifers), Paracentrotus lividus (Echinoderms)	Considering the high levels of sediment contamination highlighted from chemical analysis, an unexpected very low toxic effect was observed, even considering the sub-lethal end-point (larval swimming speed alteration).Immobility and swimming speed alteration were found.	Costa et al., 2016 [139]

Notes: Standard mix of 16 representative PAHs*: acenaphthene, acenaphthylene, anthracene, benzo[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*g*,*h*,*i*]perylene, benzo[a]pyrene, chrysene, dibenz[*a*,*h*]anthracene, fluoranthene, fluorene, indeno[*1*,*2*,*3-c*,*d*]pyrene, naphthalene, phenanthrene, and pyrene; CAT: catalase, GPx: glutathione peroxidases; GST: glutathione S-transferase, and GR: glutathione reductase; K_{ow}: n-Octanol/Water Partition Coefficient; MPs: microplastics; PE: polyethylene; PHM: polyhydroxybutyrate; SOD: superoxide dismutase.

As it has been well established in the literature, marine microalgae are the primary producers of marine ecosystems that have often been used for the evaluation of environmental effects and toxicity of a wide range of chemical pollutants due to several different advantages, among which their small size, rapid growth and reproduction, and great sensitivity are included [130]. For all of the aforementioned reasons, the scientific research focusing on the impacts of oil pollution on these organisms (that are the base of the marine food chain) is a field that has been extensively researched worldwide in the scientific community [131]. Especially due to the characteristic of PAHs to be subjected under low biodegradation, combined with their ability to be bioaccumulated through the marine food webs, makes the effects on phytoplanktonic species of those pollutants more important for the fate and magnification capacity of PAHs in higher trophic levels [132].

Polychlorinated biphenyls (PCBs) are compounds that were widely produced in the industrialized countries during the 20th century that were used as dielectric fluid in electric transformers and capacitors, plasticizers, etc. PCBs currently are substances of particular concern since their continuous detection in various environmental compartments such as fatty tissues and sediments became known.

According to the found and reviewed bibliography herein, marine microalgal bioassays have been conducted with sediments or sediment extracts containing PAHs, although for some microalgal species an induced inhibition of algal growth and a decrease of biomass and Chlorophyll-a (Chl-a) content has been observed, such as in *Dunaliella tertiolecta*, *Isochrysis galbana*, and *Phaeodactylum tricornutum*, for which inhibitions of microalgal growth were observed for fractions of aromatics with log K_{ow} 5–6, esterase activity and cell membrane integrity [130]. However, for some other microalgal species, contradictory results were reported since those species tolerated PAHs and therefore resisted the toxic effects of the same toxicants through accumulating and biodegrading mechanisms [131,140,141]. For instance, Bretherton et al. (2020) [141] reported that whereas growth and photosynthetic response of microalgal species *Micromonas pusilla*, and *Prorocentrum minimum* was sensitive to oil and dispersant exposure, three other tested microalgal species *Tetraselmis astigmatica*, *Ochromona* sp., and *Heterocapsa pygmaea* were resistant under the same exposure conditions. Furthermore, cell size was reported to be the most important factor in determining the biomass response to oil, whereas motility/mixotrophy was the more important parameter in the dispersed oil [141].

Similarly, large algae, such as species of diatoms, have been observed to possess the capacity to tolerate PAHs exposure. For example, in a study conducted by Melliti Ben Garali et al. (2021) [131], the diatoms *Pseudo-nitzschia mannii* and *Pseudo-nitzschia hasleana* that were isolated from a PAH contaminated marine environment not only maintained their growth in non-axenic cultures (in the presence of 15 PAHs in mixture up to concentration level of 120 μg L^{-1} and 144-h exposure) but increased the cell biovolume as well, and the greater increase was revealed to occur for P. *mannii* [131]. Other PAHs tolerating diatoms

species are *Skeletonema costatum*, *Phaeodactylum tricornutum*, *Chaetoceros* sp., and *Nitzschia* sp. [142–145].

Even though the majority of researchers have mainly focused on the carcinogenic toxicity of PAHs on organisms, the more recent surveys have revealed the toxic effects of those pollutants on marine biota, including endocrine disruptions and tissue-specific toxicity of exposed aquatic animals. Among the most commonly observed disturbances and various harmful effects on marine organisms (including fish, benthic organisms, and invertebrates), developmental toxicity (heart developmental anatomy on cardiotoxicity-based adverse outcome pathways, ocular development, etc.), genotoxicity, immunotoxicity, oxidative stress, and endocrine disruptions have been reported [146–149]. More specifically, the impacts of petroleum-derived pollutants and PAHs on fish development and the wide diversity of health implications have been studied and reviewed by a number of researchers [146,150,151]. Moreover, the differential toxicokinetics of PAHs in embryos of Atlantic haddock and cod have been exhibited by Sørensen et al. (2017) [152]. Toxicity to immune system functions, inflammatory responses, and estrogen and androgen metabolic pathways on male tilapia by benzo(a)pyrene exposure was reported by Colli-Dula et al. (2018) [153]. The toxicity of PAHs on the bone metabolism of fish has been investigated by Ikegame et al. (2019) [146] and Honda and Suzuki et al. (2020) [154].

Furthermore, LMW-PAHs, such as naphthalene and three-ring PAHs, are accumulated in both fish and invertebrates as shown in common sole (*Solea solea*) tissues from the North Adriatic Sea peculiar impacted area [155]. Due to PAHs lipophilic character, total PAHs concentration in several organisms' tissues are positively correlated with lipid content of specific tissues, as indicated by Ranjbar Jafarabadi et al. (2019) [156] and Yu et al. (2019) [157]. However, this was not confirmed by Frapiccini et al. (2018) [155], and Soltani et al. (2019) [158], who reported either extremely weak positive correlations or no correlations between lipid content and PAH concentrations in the tissues of fish such as liver and testes.

Several invertebrates such as wharf roach *Ligia* sp. [159] and blue crab *Portunus segnis* from the Persian Gulf [160] have been studied regarding accumulation and pollution surveys for the biomonitoring of PAHs [146].

Aquatic fauna including marine reptiles are susceptible to LMW-PAHs, which are chemical compounds with the tendency to remain in the water and thus be bioavailable for biological uptake [161]. According to a recent review by Ruberg et al. (2021) [161] regarding the impacts of petroleum toxicity in marine reptiles, and specifically marine turtles and iguanas, and focusing on research data related to physiology and fitness toxicological effects, it was stated that these organisms play a key role in the balance of trophic webs due to their ectothermic nature that enables them to have slow metabolisms and therefore makes them sensitive to xenobiotics [161]. Multiple routes of exposure have been reported for marine turtles, such as inhalation of air from the sea surface layer that contains vaporized PAHs, while after diving, consumption of contaminated prey (e.g., invertebrates, mollusks) can lead to the bioconcentration of PAH toxicants, therefore *Lepidochelys kempii* (Kemp's ridleys) and loggerhead turtles are at higher risk of exposure to PAHs than the *Chelonia mydas* (herbivorous green turtle) [162].

Based on the reported data, the most common effects of petroleum and crude oil on marine reptiles (turtles and iguanas) include: (i) modifications of skin function, immune responses, energy metabolism, respiration, and diving patterns of adult turtles, (ii) hatchling deformities in exposed eggs, altered incubation duration, and decreased embryonic survival, (iii) decrease of body mass and modification of clinical pathology parameters, and (iv) increased corticosterone levels in marine iguanas and wipe out of gut bacteria [163–168].

Peer-reviewed literature on the chronic and catastrophic petroleum spillage and conventional crude oil on marine mammals has been conducted by Ruberg et al. (2021) [169], and based on the reviewed findings the observed effects include: (i) genotoxicity, (ii) modulations of immune function and/or organ weight, (iii) hematological injury, (iv) neurotoxicity, (v) metabolic and clinical abnormalities, (vi) lung disease, (vii) eye irritation,

(viii) decreased reproductive success, (ix) behavioral impacts, (x) population-level declines, and (xi) mortality [169]. Both polluted seawater and marine sediments are marine mammals' habitats for potential exposure to PAH because apart from their incidental ingestion at the sea surface (air-water interface), concentrated quantities of sinking PAHs adsorbed onto organic sediment particles can be found as well. Direct contact and inhalation through blowholes, nasal turbinates, and air-filtering cilia are some of the ways through which marine mammals can be contaminated, whereas when absorbed into the circulation of marine mammals those compounds can attack the liver, blood-forming tissues, and nervous system. Persistent lung disease and impaired stress response [170], immunotoxic effects [171,172], bacterial pneumonia, adrenal dysfunction, DNA damages, lethargy, reduced reproductive success, and mortality have been observed and reported in marine cetaceans, such as bottlenose dolphins [169,170,173,174]. Metabolic stress and hypothermia, which most commonly result in death, are the effects on marine fissipeds [169].

Finally, it is worth mentioning that according to the reviewed data, during the last 5.5 years the synergistic impacts of some specific PAHs and MPs on some marine organisms have been investigated, and among the several other published studies are included the cases of anthracene or phenanthrene with PE (2 and 20 mg g^{-1} marine sediment) where decreased effects on the bacterial community were reported by Kleinteich et al. (2018) [94]. This is in accordance with the results of Li et al. (2020) [30], who reported decreased early developmental toxicity of phenanthrene on *Oryzias melastigma* (marine medaka) with the co-presence of a low level of PE-MPs. Similarly, González-Soto et al. (2019) [91] observed increased effects of MPs-benzo[*a*]pyrene compared to MPs alone in hemocyte viability and catalase activity and in digestive gland structure of exposed mussels *Mytilus galloprovincialis*, while size-dependent impacts of MP were revealed on DNA damage and cell-type composition of digestive tubules. The synergistic immunotoxic impact of benzo[*a*]pyrene on bivalve species *Tegillarca granosa* was generally aggravated by smaller MPs (500 nm) and mitigated by larger ones (30 mm) [92]. Another case of a study investigating the synergistic effects of PAHs and MPs is the study of Magara et al. (2019) [93], who surveyed the impacts of combined exposures of fluoranthene and polyethylene or polyhydroxybutyrate (which is an eco-friendly substitute to plastic and more biodegradable) MPs on oxidative stress biomarkers in the blue mussel (*Mytilus edulis*). Based on the acquired results of co-exposure and incubation treatments, it was suggested that there was an apparent absence of combined effects [93].

3.4. Pesticides

Pesticides, also known as agrochemicals or plant protection products, are chemical compounds that are designed to be used as plant protection products. They are applied in the field for the protection of plants against pests, weeds, and several diseases that affect and decrease the quantity and quality of agricultural crop products. Globally, approximately 3.5 million tons of pesticides are used each year, mainly for agricultural and secondly for non-agricultural and urban purposes [175]. Therefore, an expansive range of synthetic organic pesticides belonging to different chemical classes, possessing diverse physicochemical properties, and targeting multiple and dissimilar pests are available on the market.

Based on several different criteria, pesticides can be subdivided into many categories. For instance, on the basis of their chemical structure, the groups of anilides, amides, organophosphates, organothiophosphates, carbamates, benzothiazoles, triazines, neonicotinoids, organochlorines, and many other chemical classes are determined. On the basis of the target organism against which they are applied, the classes of acaricides, fungicides, herbicides, insecticides, nematicides, and plant growth regulators are included, among many others. Finally, according to the World Health Organization (WHO) pesticides are classified into five classes based on the risk and hazard towards non-target organisms and ecosystems: extremely hazardous (Class Ia), highly hazardous (Class Ib), moderately

hazardous (Class II), slightly hazardous (Class III), and unlikely to present acute hazard (Class U) [176].

After their introduction, predominantly into the terrestrial environment, they can enter aquatic environmental bodies through alternative pathways such as diffuse processes, surface runoff, leaching, erosion, spray-drift, and atmospheric deposition after their volatilization. The distribution of pesticides between soil, water, air, and biota matrices determines their bioavailability and their environmental fate. Consequently, non-target organisms are often susceptible to pesticides due to the conserved nature of biochemical pathways across taxa, even though they are designed and marketed to target pest species [175].

Furthermore, to this point it must be mentioned that several xenobiotics such as pesticides that are applied in terrestrial agriculture, are simultaneously contained in the plant materials that are used for the replacement of marine ingredients in the feeds supplied in fish farms and can be introduced in the marine environment, affecting not only fishes but also other marine organisms [177]. According to the relevant literature, insecticides and herbicides are two groups of pesticides that are most frequently detected in river catchments, coastal waters, and in intertidal and subtidal marine environments.

The wide variety of effects observed in non-target species exposed to pesticides include detrimental impacts to biota with photosynthetic symbionts (e.g., marine microalgae *Rhodomonas salina* [178], diatoms *Phaeodactylum tricornutum* [179] and *Chaetoceros muelleri* [180], tropical marine cnidarian, sea anemones *Exaiptasia pallida* and symbiotic zooxanthellae microalga *Symbiodinium* spp. [181], *Cassiopea maremetens* medusae [182]), but also disruptions to non-photosynthetic animals such as reduced growth and reproduction rates of invertebrates (e.g., sea urchin *Paracentrotus lividus* [183]) and vertebrates (Pacific oyster *Crassostrea gigas* [184] and Sheepshead minnow *Cyprinodon variegatus* [185]), disruptions of nerve impulses which can ultimately lead to paralysis and death of invertebrates, and several sub-lethal effects on physiological or metabolic endpoints that are usually measured during the exposure treatments and provide unambiguous information about responses to pesticide exposure [175,186,187].

Table 4 illustrates summarized information gathered in selected recent and reviewed studies regarding the evaluation of pesticide toxicity on marine plant and animal species during the period from 1 January 2016 to 30 June 2021.

Table 4. Selected studies evaluating the toxicity of pesticides on marine plant and animal species.

Pesticide(s)	Tested Species	Main Findings	Reference
Glyphosate formulation (Roundup)	Natural communities of marine microphytobenthos	The tests indicated that microphytobenthic communities were relatively resistant to herbicide. The species richness of the communities probably enabled them to rebuild effectively. Sensitive species were replaced by those more tolerant of glyphosate. Only at the highest glyphosate concentration (8.5 g·dm^{-3}) tested was a strong negative effect noted that limited community abundance and eliminated some of the organisms. The dominant diatoms in the communities were replaced by intensively developing cyanobacteria, which ultimately comprised nearly 60% of all the cells observed in the communities.	Sylwestrzak et al., 2021 [188]
Dichlorvos, Malathion, Trichlorfon, Azamethiphos, Pyrethrum, Cypermethrin, Deltamethrin, Ivermectin, Emamectin, Benzoate, Doramectin, Teflubenzuron, Diflubenzuron	*Macrocystis pyrifera* (Giant kelp) fronds, *Atherinops affinis* and *Mysidopsis bahia* (Top smelt), *Mytilus galloprovincialis* (Blue mussels), *Strongylocentrotus purpuratus* (Purple sea urchins), *Platichthys stellatus* (Juvenile starry flounder), *Gasterosteus aculeatus* (Three-spined stickleback), *Clinocottus globiceps* (Mosshead sculpin) juveniles	No susceptibility trend for any species tested, or inherent toxicity trend for any chemical was seen. Toxicological parameters indicate that recommended treatment concentrations may result in non-target organism toxicity. No susceptibility trend for any species, or inherent toxicity trend for any chemical, although DM tended to be the most toxic and HP the least toxic to the majority of species (macroalgae, echinoderms, bivalves, crustaceans and fish).	Strachan and Kennedy, 2021 [189]

Table 4. *Cont.*

Pesticide(s)	Tested Species	Main Findings	Reference
Glyphosate, and its commercial solution (Roundup), Isoproturon, Nicosulfuron, Chlortoluron, Boscalid.	*Crassostrea gigas* (Pacific oyster)	Effects on development, growth and swimming activity were recorded. The six pesticides induce developmental defects at moderate and high concentrations. Several pesticides affect growth and/or swimming behavior of larvae. Chlortoluron, boscalid and glyphosate represent a risk for oyster embryos in the Pertuis Charentais.	Bringer et al., 2021 [184]
Atrazine	*Cyprinodon variegatus* (Sheepshead minnow)	Atrazine slightly to moderately toxic towards *C. variegatus* under acute conditions. The acute 96-h LC_{50} was 13 mg L^{-1} and no sub-lethal effects observed up to 3.2 mg L^{-1}. In the 33-d early-life stage test, no effects on survival up to 2.2 mg L^{-1}. Reduced growth at 2.2 mg L^{-1}, but this exceeds environmental concentrations.	Brain et al., 2021 [185]
Glyphosate (individual and combined effects of glyphosate and PS-MPs)	*Salvinia cucullata* (Floating plant)	Polystyrene microplastics and glyphosate had ecotoxicity effects on *S. cucullate*, caused physical damage, oxidative stress accumulation. Both single and synergistic effects on leaf growth was observed.	Yu et al., 2021 [190]
Clothianidin, Thiacloprid, Imidacloprid, Thiamethoxam	*Nitocra spinipes* (Brackish copepod)	Acute toxicity testing revealed that immobilization is a more sensitive endpoint than mortality, with 96-h median effect concentration (EC_{50}-96h) values of 6.9, 7.2, 25, and 120 μg L^{-1} for clothianidin, thiacloprid, imidacloprid, and thiamethoxam, respectively. The larval development tests resulted in 7-d no-observed-effect concentrations (NOECs-7d) of 2.5, 2.7, 4.2, and >99 μg L^{-1} for clothianidin, thiacloprid, imidacloprid, and thiamethoxam, respectively.	Moeris et al., 2021 [191]
Warfarin sodium	*Pelodiscus sinensiss* (Oftshell turtles), *Trachemys scripta elegans* (Red-eared slider turtles)	Green sea turtles metabolized warfarin very slowly. Intravenous administration of warfarin caused prothrombin time prolongation in sea turtles. Vitamin K epoxide reductase was inhibited in turtles. In vitro assay revealed interspecific differences in warfarin metabolism among different turtle species.	Yamamura et al., 2021 [192]
Metazachlor	*Prorocentrum minimum* (Dinoflagellate, marine phototrophs)	Metazachlor significantly decreased cell growth and pigment levels, and damaged chloroplast integrity, malfunctioning photosynthesis in *P. minimum* to lead to cell death. Treatment with melolachlor increased photosynthesis genes expression, destroying the chloroplast structure. Antioxidant *PmGST* induced by tested pesticide with ROS production, but *PmKatG* was not different.	Kim et al., 2021 [193]
Chlorpyrifos (Individual and combined effects of chlorpyrifos and PE-MPs)	*Acartia tonsa* (Marine copepod)	PE-MPs increased chlorpyrifos toxicity to copepods. Chlorpyrifos-loaded MPs showed higher toxicity (LC_{50} = 0.26 μg L^{-1}) than dissolved chlorpyrifos (LC_{50} = 1.34 μg L^{-1}).	Bellas et al., 2020 [26]
Dichlorvos	*Ruditapes decussatus* (Marine bivalves, Mollusks, Commercial clam)	Results showed that 0.05 mg L^{-1} of dichorvos induced oxidative stress and neurotoxicity in R. *decussatus* after 2 days of exposure.	El Ayari et al., 2020 [194]
Diuron, Propazine, Tebuthiuron, Haloxyfop	*Chaetoceros muelleri* (Marine diatom)	The effect concentrations, which reduced ΔF/Fm′ value by 50% (EC_{50}), ranged from 4.25 μg L^{-1} (diuron) to 48.6 μg L^{-1} (propazine), while the EC_{50}s for SGR were on average threefold higher, ranging from 12.4 μg L^{-1} (diuron) to 187 μg L^{-1} (tebuthiuron). Inhibition of ΔF/Fm′ in PSII was directly linked to reduced growth in this species. In contrast, SGR and ΔF/Fm′ of *C. muelleri* were nonresponsive to the non-PSII herbicide haloxyfop at the highest concentration tested (4570 μg L^{-1}), suggesting haloxyfop does not pose a risk to *C. muelleri*.	Thomas et al., 2020 [180]
Diuron, Metribuzin, Hexazinone, Tebuthiuron, Bromacil, Simazine, Propazine, Imazapic, Haloxyfop,2,4-D	*Rhodomonas salina* (Marine microalgae)	Experimental exposures to seven individual PSII inhibitor herbicides (diuron, metribuzin, hexazinone, tebuthiuron, bromacil, simazine, propazine) led to inhibition of ΔF/Fm′ and subsequent reductions in SGR. On the contrary, the three non-PSII inhibitor herbicides (imazapic, haloxyfop and 2,4-D) caused low or no toxic responses to the function of the PSII or growth at the highest concentrations tested, suggesting these herbicides pose little risk to *R. salina*.	Thomas et al., 2020b [178]

Table 4. *Cont.*

Pesticide(s)	Tested Species	Main Findings	Reference
Glyphosate-based Roundup	*Phaeodactylum tricornutum* (Marine diatom)	High concentrations decreased cell density. Furthermore, inhibition of photosynthetic activity was not only caused by the impairment of electron transport in the thylakoids, but also by a decrease of antioxidant capacity and increased lipid peroxidation. Pigment composition and fatty acid profiles proved to be efficient biomarkers for the highest glyphosate-based herbicide concentrations.	de Carvalho et al., 2020 [179]
Glyphosate, its commercial formulation Roundup, and AMPA	*Paracentrotus lividus* (Sea urchin)	The effects on larval development, growth and metabolism were assessed during 48 h of exposure from the time of egg fertilization. The results confirm that AMPA and its parent compound, glyphosate have similar toxicity, as observed in other marine invertebrates. However, interestingly, the Roundup formulation seemed to be less toxic than the glyphosate alone.	Asnicar et al., 2020 [183]
Atrazine and Chlorpyrifos	*Aurelia aurita* (Jellyfish)	The chronic exposure to current Australian water quality guideline values of atrazine and chlorpyrifos, either individually or in combination, has no effect on the survival or metabolome content of *Aurelia aurita* polyps.	Olguín-Jacobson et al., 2020 [175]
Chlorpyrifos, Chlorpyrifos oxon, Diazinon, Carbaryl	*Artemia salina* (Marine crustaceans)	*A. salina* cyst exposure to low doses of cholinergic pesticides affects hatching and larvae viability. Larval survival changes, and decreased AChE activity were observed.	Gambardella et al., 2018 [195]
Atrazine (individual and combined effects of mixtures with Carbamazepine, and Bisphenol A)	*Perna viridis* (Marine bivalves, Green mussels)	3 of the 10 biomarkers tested on green mussels (genotoxicity, inhibition of AchE, and EROD) responded after exposure to atrazine at environmentally relevant doses or below, and confirmed the potency of this herbicide to marine bivalves. Exposure tests using mixtures of atrazine, carbamazepine and Bisphenol-A also revealed that these 3 substances were generally acting in an additive manner on the selected biomarkers, at environmental doses, with some exceptions (antagonism and/or synergy) at low and high concentrations.	Juhel et al., 2017 [196]
Monocrotophos	*Hemicentrotus pulcherrimus* (Sea urchin, Echinoderms)	Pesticide disrupted the expression of netrin patterns during embryogenesis and changes in its receptor neogenin expression during early development had a similar tendency with that of netrin. Monocrotophos may disturb development of serotonergic system via a netrin-dependent pathway.	Zhang et al., 2017a [197]

NOTES: AChE: acetylcholinesterase; AMPA: aminomethylphosphonic acid; 2,4-D: 2,4-Dichlorophenoxyacetic acid; EC_{50}: effective concentration; EROD: 7-ethoxyresorufin O-deethylase; LC_{50}: lethal concentration; NOECs: no-observed-effect concentrations; $\Delta F/F_m'$: effective quantum yield; MPs: microplastics; PE: polyethylene; PSII: Photosystem II, *PmGST* and *PmKatG:* photosynthesis genes; ROS: reactive oxygen species; SGR: specific growth rates.

Interestingly, in a recent review by Deidda et al. (2021) [186] focusing on the neurotoxic effects of several emerging pollutants in marine invertebrates, it is reported that even if studies on pollutants' neurotoxic effects are still few, marine invertebrates are used in ecotoxicological studies as model systems regarding the impacts of xenobiotics such as pesticides on the nervous system. Organochlorines, organophosphates, and carbamates are three classes of pesticides that are known for their neurotoxic effects on marine organisms, invertebrates, and vertebrates [186,187]. Although the use of many organochlorinated pesticides which are chlorinated hydrocarbon derivatives has been banned in developed countries due to their high toxicity and long environmental persistence, they are used in other non-developed countries. On the contrary, the substitutes of organochlorine pesticides currently used are both organophosphates, which are synthetic compounds containing at least one phosphate ester group, and carbamates, which are derived from carbamic acid, and are considered as less hazardous and more (bio)degradable compounds. They target the cholinergic system of exposed organisms, and their mode of action is based on their ability to inhibit the acetylcholinesterase (AchE) activity via binding the enzyme active site in an irreversible manner.

Sea urchin embryos and larvae have been employed in the toxicity assessment tests conducted to evaluate the neurotoxicity of pesticides on marine echinoderms. For example, Zhang et al. (2017) [197] observed ubiquitous disruptions of all the neurotransmitter pathways leading to adverse effects on larval morphogenesis of sea urchin *Hemicentrotus pulcherrimus* after the exposure to different concentrations (0.01, 0.10, and 1.00 mg L^{-1}) of the organophosphorus insecticide monocrotophos. Moreover, monocrotophos induced disruptions in the expression of the netrin patterns during embryogenesis, which is a chemotropic axon guidance cue, and changes in its receptor neogenin during early development of the same species (*Hemicentrotus pulcherrimus*), and are revealed in the bibliography [197].

According to the recently published research of El Ayari et al. (2020) [194], the detoxifying effect of *Polygonum equisetiforme* extracts against dichlorvos induced oxidative stress and neurotoxicity in the commercial clam *Ruditapes decussatus*. Acquired results showed that even at the lower tested exposure level (0.05 mg L^{-1}) and exposure for two days oxidative stress was induced which resulted in the reduction of AChE activity, whereas the greatest toxic effects were observed at 0.25 mg L^{-1} when significant changes of the several biochemical markers analyzed were reported to be caused [194].

Among the various different toxic effects induced by atrazine, either tested alone or in mixtures with bisphenol A (plasticizer) and carbamazepine (pharmaceutical) on green mussels, Juhel et al. (2017) [196] evaluated *Perna viridis* and found changes in mussel immune functions, significant alterations of DNA damage biomarkers, detoxification enzyme Ethoxyresorufin-O-Deethylase, severe inhibition of haemolymph AChE activity, increase of the total number of haemocytes, and a decrease in their phagocytic activity [196].

The impacts of chlorpyrifos on the crustacean *Litopenaeus vannamei* were investigated by Duarte-Restrepo et al. (2020) [198], and after the exposure of adult shrimp to sub-lethal concentration levels of chlorpyrifos (0.7 and 1.3 µg/L) for 96 h, significant alterations in the lipid oxidation levels, antioxidant enzymes activities, and AChE activity were revealed. After the exposure of Artemia salina (cyst stage) to a variety of pesticides (chlorpyrifos oxon, diazinon, and carbaryl) at concentration levels 10^{-11}–10^{-5} M (similar to those found in a contaminated coastal environment), for long exposure times (72, 96, and 192 h), significant alterations in the hatching speed and larval survival were observed, according to the published work of Gambardella et al. (2018) [195]. Moreover, decreased ChE activity at 96 h in the protocerebrum, a brain segment that is associated with vision, were revealed in the same survey.

The toxicity of several different antifouling biocides to marine species has been recently reviewed by de Campos et al. (2021) [6], and among the various data reported: diuron 10 d-LC_{50} = 5 mg L^{-1} for the cnidarian *Aurelia aurita* [199]; dichlofluanid 96 h-EC_{50} = 377 mg L^{-1} for the diatom *Nitzschia pungens* [200], and 48 h-LC_{50} = 154,000 mg L^{-1} for the microcrustacean *Artemia* sp. [200]; zinc pyrithione 96 h-EC_{50} = 280 mg L^{-1} for the microalgae *Tetraselmis chuii* [201], and 72 h-LC_{50} = 3200 mg L^{-1} for the bivalve *Mytilus galloprovincialis* [202]; copper pyrithione 72 h-EC_{50} = 3200 mg L^{-1} for the bivalve *Mytilus galloprovincialis* [202], and LC_{50} = 3800 mg L^{-1} for the bivalve *Mytilus galloprovincialis* [202]; medetomidine 48 h-LC_{50} = 48.3 mg L^{-1} for the copepod *Acartia tonsa* [203]; zineb 96 h-EC_{50} = 232 mg L^{-1} for the diatom *Nitzschia pungens* [200]; 96 h-LC_{50} = 29 mg L^{-1} for the fish species *Pagrus major* [204]; and 48 h-LC_{50} = 41 mg L^{-1} for *Artemia* sp. [200].

4. Conclusions

Numerous toxic and persistent organic molecules can be found in the marine environment, interact with their surroundings, and cause diverse lethal and sub-lethal effects on marine biota and marine ecosystems. The present review presents the recent research that has been conducted during the period from 1 January 2016 to 30 June 2021 concerning the toxicity of selected chemical groups of POPs, and more specifically: (i) microplastics, nanoplastics, and plastic-derived chemicals, (ii) pharmaceutical drugs, (iii) PAHs and PCBs, and (iv) pesticides.

According to the findings of the current review, a wide interest is observed to arise within the scientific community regarding PCBs, PAHs, pesticides, pharmaceuticals, MPs, NPs, and other plastic-derived chemicals and their potential effects on an extended variety of marine species. Based on the gathered and reviewed data herein that were retrieved from "Scopus", "Google Scholar", "SpringerLink", and "Open Access Journal Search Engine", an undiminished scientific interest is revealed that is focused on the impacts of POPs on many marine organisms, both invertebrates and vertebrates, which may take part in the human food chain and, along with environmental pollution, can potentially provoke harmful and hazardous impacts to human health.

The retrieved bibliographic data after their classification into the relevant categories revealed that, in recent years, the majority of the studies (≈28%) are dealing with pharmaceuticals, followed by pesticides/agrochemicals (≈24%), PAHs (≈21%), microplastics and plastic-derived chemicals (≈17%), and PCBs (≈10%). A constantly growing number of studies regarding the effects of several types and sizes of MPs, NPs, and plastic-derived chemicals was also observed.

Acquired results showed that during the last 5.5 years several research studies have focused on the induced and responding mechanisms of the antioxidant system in multiple tissues of marine mussels (especially the edible species *Mytilus galloprovincialis*) after exposure to all the selected toxicants (MPs, NPs, pharmaceuticals, PAHs, PCBs, and pesticides). Therefore, these sessile, sensitive, and globally distributed organisms can be characterized as excellent bioindicators to a wide variety of environmental POPs stressors. Their crucial ecological role, due to their unique filter-feeding lifestyle, makes them susceptible to waterborne contaminants.

It must be highlighted the fact that even though a large number of published data exist on the impacts of selected anthropogenic toxicants on different species of marine organisms, the concentration levels used in the conducted studies evaluating the ecotoxicological and physiological risks due to the exposure of marine biota species to several POPs need to be environmentally relevant, so that acquired data can be harmonized. It will therefore be possible to clearly compare the effects of those toxicants in marine biota.

Furthermore, although the synergistic impacts of some specific POPs that belong to different groups, such as PAHs and MPs or pesticides and MPs, on some marine organisms have already been investigated, corresponding surveys regarding a variety of combinations and new mixtures of toxicants that can penetrate the sea system and contaminate global oceans should be conducted in the future. Moreover, clearly further work is required to elucidate the combined effects on marine and estuarine species and simultaneous climate-related changes (temperature rise and ocean acidification scenario) and chemical POPs stress that might change the marine organisms' sensitivity towards them.

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References

1. Thiel, H. Anthropogenic impacts on the deep sea. In *Ecosystems of the World*; Tyler, P.A., Ed.; Elsevier Science: Amsterdam, The Netherlands, 2003; Volume 28, pp. 427–471.
2. Alfaro-Núñez, A.; Astorga, D.; Cáceres-Farías, L.; Bastidas, L.; Villegas, C.S.; Macay, K.; Christensen, J.H. Microplastic pollution in seawater and marine organisms across the Tropical Eastern Pacific and Galápagos. *Sci. Rep.* **2021**, *11*, 1–8. [CrossRef] [PubMed]
3. Elizalde-Velázquez, G.A.; Gómez-Oliván, L.M. Microplastics in aquatic environments: A review on occurrence, distribution, toxic effects, and implications for human health. *Sci. Total Environ.* **2021**, *780*, 146551. [CrossRef] [PubMed]

4. Alygizakis, N.A.; Gago-Ferrero, P.; Borova, V.L.; Pavlidou, A.; Hatzianestis, I.; Thomaidis, N.S. Occurrence and spatial distribution of 158 pharmaceuticals, drugs of abuse and related metabolites in offshore seawater. *Sci. Total Environ.* **2016**, *541*, 1097–1105. [CrossRef] [PubMed]
5. Patel, M.; Kumar, R.; Kishor, K.; Mlsna, T.; Pittman, C.U., Jr.; Mohan, D. Pharmaceuticals of emerging concern in aquatic systems: Chemistry, occurrence, effects, and removal methods. *Chem. Rev.* **2019**, *119*, 3510–3673. [CrossRef]
6. De Campos, B.G.; Figueiredo, J.; Perina, F.; Abessa, D.M.D.S.; Loureiro, S.; Martins, R. Occurrence, effects and environmental risk of antifouling biocides (EU PT21): Are marine ecosystems threatened? *Crit. Rev. Environ. Sci. Technol.* **2021**, *51*, 1–32. [CrossRef]
7. Ajith, N.; Arumugam, S.; Parthasarathy, S.; Manupoori, S.; Janakiraman, S. Global distribution of microplastics and its impact on marine environment—A review. *Environ. Sci. Pollut. Res.* **2020**, *27*, 25970–25986. [CrossRef] [PubMed]
8. Gonçalves, J.M.; Bebianno, M.J. Nanoplastics impact on marine biota: A review. *Environ. Pollut.* **2021**, *273*, 116426. [CrossRef]
9. Mallik, A.; Xavier, K.M.; Naidu, B.C.; Nayak, B.B. Ecotoxicological and physiological risks of microplastics on fish and their possible mitigation measures. *Sci. Total Environ.* **2021**, *779*, 146433. [CrossRef]
10. Boucher, J.; Friot, D. *Primary Microplastics in the Oceans: A Global Evaluation of Sources*; IUCN: Gland, Switzerland, 2017; pp. 1–43.
11. Ali, I.; Cheng, Q.; Ding, T.; Yiguang, Q.; Yuechao, Z.; Sun, H.; Peng, C.; Naz, I.; Li, J.; Liu, J. Micro- and nanoplastics in the environment: Occurrence, detection, characterization and toxicity—A critical review. *J. Clean. Prod.* **2021**, *313*, 127863. [CrossRef]
12. Wang, Z.; Gao, J.; Dai, H.; Zhao, Y.; Li, D.; Duan, W.; Guo, Y. Microplastics affect the ammonia oxidation performance of aerobic granular sludge and enrich the intracellular and extracellular antibiotic resistance genes. *J. Hazard. Mater.* **2020**, *409*, 124981. [CrossRef]
13. Rai, P.K.; Lee, J.; Brown, R.J.; Kim, K.-H. Micro-and nanoplastic pollution: Behavior, microbial ecology, and remediation technologies. *J. Clean. Product.* **2020**, *291*, 125240. [CrossRef]
14. Barreto, M.A.; Luis, L.G.; Girão, A.V.; Trindade, T.; Soares, A.; Oliveira, M. Behavior of colloidal gold nanoparticles in different ionic strength media. *J. Nanoparticle Res.* **2015**, *17*, 1–13. [CrossRef]
15. Sun, X.; Chen, B.; Li, Q.; Liu, N.; Xia, B.; Zhu, L.; Qu, K. Toxicities of polystyrene nano- and microplastics toward marine bacterium Halomonas alkaliphila. *Sci. Total Environ.* **2018**, *642*, 1378–1385. [CrossRef]
16. Okshevsky, M.; Gautier, E.; Farner, J.M.; Schreiber, L.; Tufenkji, N. Biofilm formation by marine bacteria is impacted by concentration and surface functionalization of polystyrene nanoparticles in a species-specific manner. *Environ. Microbiol. Rep.* **2020**, *12*, 203–213. [CrossRef]
17. M'Rabet, C.; Yahia, O.K.; Chomérat, N.; Zentz, F.; Bilien, G.; Pringault, O. Transient effect of bisphenol A (BPA) and di-(2-ethylhexyl) phthalate (DEHP) on the cosmopolitan marine diatom *Chaetoceros decipiens-lorenzianus*. *Environ. Pollut.* **2021**, *285*, 117362. [CrossRef]
18. Thiagarajan, V.; Alex, S.A.; Seenivasan, R.; Chandrasekaran, N.; Mukherjee, A. Toxicity evaluation of nano-TiO2 in the presence of functionalized microplastics at two trophic levels: Algae and crustaceans. *Sci. Total Environ.* **2021**, *784*, 147262. [CrossRef] [PubMed]
19. Bringer, A.; Thomas, H.; Dubillot, E.; Le Floch, S.; Receveur, J.; Cachot, J.; Tran, D. Subchronic exposure to high-density polyethylene microplastics alone or in combination with chlortoluron significantly affected valve activity and daily growth of the Pacific oyster, *Crassostrea gigas*. *Aquat. Toxicol.* **2021**, *237*, 105880. [CrossRef] [PubMed]
20. Hamm, T.; Lenz, M. Negative impacts of realistic doses of spherical and irregular microplastics emerged late during a 42 weeks-long exposure experiment with blue mussels. *Sci. Total Environ.* **2021**, *778*, 146088. [CrossRef] [PubMed]
21. Cormier, B.; Le Bihanic, F.; Cabar, M.; Crebassa, J.-C.; Blanc, M.; Larsson, M.; Dubocq, F.; Yeung, L.; Clérandeau, C.; Keiter, S.H.; et al. Chronic feeding exposure to virgin and spiked microplastics disrupts essential bio-logical functions in teleost fish. *J. Hazard. Mater.* **2021**, *415*, 125626. [CrossRef]
22. Venâncio, C.; Ciubotariu, A.; Lopes, I.; Martins, M.A.; Oliveira, M. Is the toxicity of nanosized polymethylmethacrylate particles dependent on the exposure route and food items? *J. Hazard. Mater.* **2021**, *413*, 125443. [CrossRef]
23. Djapovic, M.; Milivojevic, D.; Ilic-Tomic, T.; Lješević, M.; Nikolaivits, E.; Topakas, E.; Maslak, V.; Nikodinovic-Runic, J. Syn-thesis and characterization of polyethylene terephthalate (PET) precursors and potential degradation products: Toxicity study and application in discovery of novel PETases. *Chemosphere* **2021**, *275*, 130005. [CrossRef] [PubMed]
24. Sun, S.; Shi, W.; Tang, Y.; Han, Y.; Du, X.; Zhou, W.; Zhang, W.; Sun, C.; Liu, G. The toxic impacts of microplastics (MPs) and polycyclic aromatic hydrocarbons (PAHs) on haematic parameters in a marine bivalve species and their potential mechanisms of action. *Sci. Total Environ.* **2021**, *783*, 147003. [CrossRef] [PubMed]
25. Choi, J.S.; Kim, K.; Hong, S.H.; Park, K.-I.; Park, J.-W. Impact of polyethylene terephthalate microfiber length on cellular re-sponses in the Mediterranean mussel *Mytilus galloprovincialis*. *Mar. Environ. Res.* **2021**, *168*, 105320. [CrossRef]
26. Bellas, J.; Gil, I. Polyethylene microplastics increase the toxicity of chlorpyrifos to the marine copepod *Acartia tonsa*. *Environ. Pollut.* **2020**, *260*, 114059. [CrossRef]
27. Schiavo, S.; Oliviero, M.; Chiavarini, S.; Dumontet, S.; Manzo, S. Polyethylene, Polystyrene, and Polypropylene leachate impact upon marine microalgae Dunaliella tertiolecta. *J. Toxicol. Environ. Health Part A* **2020**, *84*, 249–260. [CrossRef]
28. Zhang, F.; Wang, Z.; Song, L.; Fang, H.; Wang, D.-G. Aquatic toxicity of iron-oxide-doped microplastics to *Chlorella pyrenoidosa* and *Daphnia magna*. *Environ. Pollut.* **2020**, *257*, 113451. [CrossRef]
29. Zhu, X.; Zhao, W.; Chen, X.; Zhao, T.; Tan, L.; Wang, J. Growth inhibition of the microalgae *Skeletonema costatum* under copper nanoparticles with microplastic exposure. *Mar. Environ. Res.* **2020**, *158*, 105005. [CrossRef]

30. Li, Z.; Yi, X.; Zhou, H.; Chi, T.; Li, W.; Yang, K. Combined effect of polystyrene microplastics and dibutyl phthalate on the microalgae *Chlorella pyrenoidosa*. *Environ. Pollut.* **2019**, *257*, 113604. [CrossRef] [PubMed]
31. Davarpanah, E.; Guilhermino, L. Are gold nanoparticles and microplastics mixtures more toxic to the marine microalgae *Tetraselmis chuii* than the substances individually? *Ecotoxicol. Environ. Saf.* **2019**, *181*, 60–68. [CrossRef] [PubMed]
32. Thiagarajan, V.; Iswarya, V.; Seenivasan, P.A.J.R.; Chandrasekaran, N.; Mukherjee, A. Influence of differently functionalized polystyrene microplastics on the toxic effects of P25 TiO2 NPs towards marine algae *Chlorella* sp. *Aquat. Toxicol.* **2019**, *207*, 208–216. [CrossRef] [PubMed]
33. Yi, X.; Chi, T.; Li, Z.; Wang, J.; Yu, M.; Wu, M.; Zhou, H. Combined effect of polystyrene plastics and triphenyltin chloride on the green algae *Chlorella pyrenoidosa*. *Environ. Sci. Pollut. Res.* **2019**, *26*, 15011–15018. [CrossRef]
34. Rist, S.E.; Assidqi, K.; Zamani, N.P.; Appel, D.; Perschke, M.; Huhn, M.; Lenz, M. Suspended micro-sized PVC particles impair the performance and decrease survival in the Asian green mussel Perna viridis. *Mar. Pollut. Bull.* **2016**, *111*, 213–220. [CrossRef]
35. Sjollema, S.B.; Redondo-Hasselerharm, P.; Leslie, H.A.; Kraak, M.H.S.; Vethaak, A.D. Do plastic particles affect microalgal photosynthesis and growth? *Aquat. Toxicol.* **2016**, *170*, 259–261. [CrossRef] [PubMed]
36. Bergami, E.; Pugnalini, S.; Vannuccini, M.; Manfra, L.; Faleri, C.; Savorelli, F.; Dawson, K.A.; Corsi, I. Long-term toxicity of surface-charged polystyrene nanoplastics to marine planktonic species *Dunaliella tertiolecta* and *Artemia franciscana*. *Aquat. Toxicol.* **2017**, *189*, 159–169. [CrossRef] [PubMed]
37. Venâncio, C.; Ferreira, I.; Martins, M.A.; Soares, A.M.; Lopes, I.; Oliveira, M. The effects of nanoplastics on marine plankton: A case study with polymethylmethacrylate. *Ecotoxicol. Environ. Saf.* **2019**, *184*, 109632. [CrossRef]
38. Gomes, T.; Almeida, A.C.; Georgantzopoulou, A. Characterization of cell responses in Rhodomonas baltica exposed to PMMA nanoplastics. *Sci. Total Environ.* **2020**, *726*, 138547. [CrossRef]
39. González-Fernández, C.; Le Grand, F.; Bideau, A.; Huvet, A.; Paul-Pont, I.; Soudant, P. Nanoplastics exposure modulate lipid and pigment compositions in diatoms. *Environ. Pollut.* **2020**, *262*, 114274. [CrossRef] [PubMed]
40. Ozkaleli, M.; Erdem, A. Biotoxicity of TiO2 nanoparticles on Raphidocelis subcapitata microalgae exemplified by membrane de-formation. *Int. J. Environ. Res. Public Health* **2018**, *15*, 416. [CrossRef] [PubMed]
41. Thiagarajan, V.; Ramasubbu, S.; Natarajan, C.; Mukherjee, A. Differential sensitivity of marine algae *Dunaliella salina* and *Chlorella* sp. to P25 TiO2 NPs. *Environ. Sci. Pollut. Res.* **2019**, *26*, 21394–21403. [CrossRef] [PubMed]
42. Gao, X.; Deng, R.; Lin, D. Insights into the regulation mechanisms of algal extracellular polymeric substances secretion upon the exposures to anatase and rutile TiO2 nanoparticles. *Environ. Pollut.* **2020**, *263*, 114608. [CrossRef]
43. Hou, J.; Wang, L.; Wang, C.; Zhang, S.; Liu, H.; Li, S.; Wang, X. Toxicity and mechanisms of action of titanium dioxide nano-particles in living organisms. *J. Environ. Sci.* **2019**, *75*, 40–53. [CrossRef]
44. Liu, G.; Jiang, R.; You, J.; Muir, D.C.G.; Zeng, E.Y. Microplastic Impacts on Microalgae Growth: Effects of Size and Humic Acid. *Environ. Sci. Technol.* **2019**, *54*, 1782–1789. [CrossRef] [PubMed]
45. Brandts, I.; Barría, C.; Martins, M.; Franco-Martínez, L.; Barreto, A.; Tvarijonaviciute, A.; Tort, L.; Oliveira, M.; Teles, M. Waterborne exposure of gilthead seabream (*Sparus aurata*) to polymethylmethacrylate nanoplastics causes effects at cellular and molecular levels. *J. Hazard. Mater.* **2020**, *403*, 123590. [CrossRef]
46. Manfra, L.; Rotini, A.; Bergami, E.; Grassi, G.; Faleri, C.; Corsi, I. Comparative ecotoxicity of polystyrene nanoparticles in natural seawater and reconstituted seawater using the rotifer Brachionus plicatilis. *Ecotoxicol. Environ. Saf.* **2017**, *145*, 557–563. [CrossRef] [PubMed]
47. Jeong, J.; Choi, J. Adverse outcome pathways potentially related to Hazard. identification of microplastics based on toxicity mechanisms. *Chemosphere* **2019**, *231*, 249–255. [CrossRef] [PubMed]
48. Pinsino, A.; Bergami, E.; Della Torre, C.; Vannuccini, M.L.; Addis, P.; Secci, M.; Dawson, K.A.; Matranga, V.; Corsi, I. Ami-no-modified polystyrene nanoparticles affect signalling pathways of the sea urchin (*Paracentrotus lividus*) embryos. *Nanotoxicology* **2017**, *11*, 201–209. [CrossRef] [PubMed]
49. Bergami, E.; Krupinski Emerenciano, A.; Gonzalez-Aravena, M.; Cardenas, C.A.; Hernandez, P.; Silva, J.R.M.C.; Corsi, I. Polystyrene nanoparticles affect the innate immune system of the Antarctic sea urchin *Sterechinus neumayeri*. *Polar Biol.* **2019**, *42*, 743–757. [CrossRef]
50. Silva, M.S.; Oliveira, M.; Valente, P.; Figueira, E.; Martins, M.; Pires, A. Behavior and biochemical responses of the polychaeta Hediste diversicolor to polystyrene nanoplastics. *Sci. Total Environ.* **2019**, *707*, 134434. [CrossRef]
51. Silva, M.S.S.; Oliveira, M.; Valente, P.; Figueira, E.; Martins, M.; Pires, A. Do nanoplastics impact the ability of the polychaeta Hediste diversicolor to regenerate? *Ecol. Indic.* **2020**, *110*, 105921. [CrossRef]
52. Bergami, E.; Bocci, E.; Vannuccini, M.L.; Monopoli, M.; Salvati, A.; Dawson, K.A.; Corsi, I. 2016. Nano-sized polystyrene affects feeding, behaviour and physiology of brine shrimp *Artemia franciscana* larvae. *Ecotoxicol. Environ. Saf.* **2016**, *123*, 18–25. [CrossRef]
53. Gambardella, C.; Morgana, S.; Ferrando, S.; Bramini, M.; Piazza, V.; Costa, E.; Garaventa, F.; Faimali, M. Effects of polystyrene microbeads in marine planktonic crustaceans. *Ecotoxicol. Environ. Saf.* **2017**, *145*, 250–257. [CrossRef]
54. Bhargava, S.; Lee, S.S.C.; Ying, L.S.M.; Neo, M.L.; Teo, S.L.-M.; Valiyaveettil, S. Fate of Nanoplastics in Marine Larvae: A Case Study Using Barnacles, *Amphibalanus amphitrite*. *ACS Sustain. Chem. Eng.* **2018**, *6*, 6932–6940. [CrossRef]
55. Bergami, E.; Manno, C.; Cappello, S.; Vannuccini, M.; Corsi, I. Nanoplastics affect moulting and faecal pellet sinking in Antarctic krill (*Euphausia superba*) juveniles. *Environ. Int.* **2020**, *143*, 105999. [CrossRef]

56. Balbi, T.; Camisassi, G.; Montagna, M.; Fabbri, R.; Franzellitti, S.; Carbone, C.; Dawson, K.; Canesi, L. Impact of cationic polystyrene nanoparticles (PSNH2) on early embryo development of *Mytilus galloprovincialis*: Effects on shell formation. *Chemo-sphere* **2017**, *186*, 1–9. [CrossRef]
57. González-Fernández, C.; Tallec, K.; Le Goïc, N.; Lambert, C.; Soudant, P.; Huvet, A.; Suquet, M.; Berchel, M.; Paul-Pont, I. Cellular responses of Pacific oyster (*Crassostrea gigas*) gametes exposed in vitro to polystyrene nanoparticles. *Chemosphere* **2018**, *208*, 764–772. [CrossRef] [PubMed]
58. Jovanović, B.; Gökdağ, K.; Guven, O.; Emre, Y.; Whitley, E.M.; Kideys, A.E. Virgin microplastics are not causing imminent harm to fish after dietary exposure. *Mar. Pollut. Bull.* **2018**, *130*, 123–131. [CrossRef] [PubMed]
59. Mattsson, K.; Johnson, E.V.; Malmendal, A.; Linse, S.; Hansson, L.-A.; Cedervall, T. Brain damage and behavioural disorders in fish induced by plastic nanoparticles delivered through the food chain. *Sci. Rep.* **2017**, *7*, 1–7. [CrossRef]
60. Chen, Q.; Yin, D.; Jia, Y.; Schiwy, S.; Legradi, J.; Yang, S.; Hollert, H. Enhanced uptake of BPA in the presence of nanoplastics can lead to neurotoxic effects in adult zebrafish. *Sci. Total Environ.* **2017**, *609*, 1312–1321. [CrossRef] [PubMed]
61. Skjolding, L.M.; Asmonaite, G.; Jølck, R.I.; Andresen, T.L.; Selck, H.; Baun, A.; Sturve, J. An assessment of the importance of exposure routes to the uptake and internal localisation of fluorescent nanoparticles in zebrafish (*Danio rerio*), using light sheet microscopy. *Nanotoxicology* **2017**, *11*, 351–359. [CrossRef] [PubMed]
62. Chae, Y.; An, Y.-J. Effects of micro- and nanoplastics on aquatic ecosystems: Current research trends and perspectives. *Mar. Pollut. Bull.* **2017**, *124*, 624–632. [CrossRef]
63. Pitt, J.A.; Trevisan, R.; Massarsky, A.; Kozal, J.S.; Levin, E.D.; Di Giulio, R.T. Maternal transfer of nanoplastics to offspring in zebrafish (*Danio rerio*): A case study with nanopolystyrene. *Sci. Total Environ.* **2018**, *643*, 324–334. [CrossRef]
64. Lee, S.; Gounley, J.; Randles, A.; Vetter, J.S. Performance portability study for massively parallel computational fluid dynamics application on scalable heterogeneous architectures. *J. Parallel Distrib. Comput.* **2019**, *129*, 1–13. [CrossRef]
65. Villalba, M.; Perez, V.; Herrera, L.; Stepke, C.; Maldonado, N.; Fredericksen, F.; Yanez, A.; Olavarría, V.H. Infectious pancreatic necrosis virus infection of fish cell lines: Preliminary analysis of gene expressions related to extracellular matrix remodeling and immunity. *Vet. Immunol. Immunopathol.* **2017**, *193–194*, 10–17. [CrossRef] [PubMed]
66. Morcillo, P.; Chaves-Pozo, E.; Meseguer, J.; Esteban, M.; Cuesta, A. Establishment of a new teleost brain cell line (DLB-1) from the European sea bass and its use to study metal toxicology. *Toxicol. In Vitro* **2017**, *38*, 91–100. [CrossRef] [PubMed]
67. Pannetier, P.; Fuster, L.; Clérandeau, C.; Lacroix, C.; Gourves, P.-Y.; Cachot, J.; Morin, B. Usefulness of RTL-W1 and OLCAB-e3 fish cell lines and multiple endpoint measurements for toxicity evaluation of unknown or complex mixture of chemicals. *Ecotoxicol. Environ. Saf.* **2018**, *150*, 40–48. [CrossRef] [PubMed]
68. Brandts, I.; Teles, M.; Tvarijonaviciute, A.; Pereira, M.D.L.; Martins, M.; Tort, L.; Oliveira, M. Effects of polymethylmethacrylate nanoplastics on Dicentrarchus labrax. *Genomics* **2018**, *110*, 435–441. [CrossRef]
69. Almeida, M.; Martins, M.A.; Soares, A.M.; Cuesta, A.; Oliveira, M. Polystyrene nanoplastics alter the cytotoxicity of human pharmaceuticals on marine fish cell lines. *Environ. Toxicol. Pharmacol.* **2019**, *69*, 57–65. [CrossRef]
70. Huang, W.; Song, B.; Liang, J.; Niu, Q.; Zeng, G.; Shen, M.; Deng, J.; Luo, Y.; Wen, X.; Zhang, Y. Microplastics and associated contaminants in the aquatic environment: A review on their ecotoxicological effects, trophic transfer, and potential impacts to human health. *J. Hazard. Mater.* **2021**, *405*, 124187. [CrossRef] [PubMed]
71. Wang, W.; Ge, J.; Yu, X. Bioavailability and toxicity of microplastics to fish species: A review. *Ecotoxicol. Environ. Saf.* **2019**, *189*, 109913. [CrossRef] [PubMed]
72. Covernton, G.A.; Davies, H.L.; Cox, K.D.; El-Sabaawi, R.; Juanes, F.; Dudas, S.E.; Dower, J.F. A Bayesian analysis of the factors determining microplastics ingestion in fishes. *J. Hazard. Mater.* **2021**, *413*, 125405. [CrossRef]
73. Wang, W.; Gao, H.; Jin, S.; Li, R.; Na, G. The ecotoxicological effects of microplastics on aquatic food web, from primary producer to human: A review. *Ecotoxicol. Environ. Saf.* **2019**, *173*, 110–117. [CrossRef]
74. Bosker, T.; Guaita, L.; Behrens, P. Microplastic pollution on Caribbean beaches in the Lesser Antilles. *Mar. Pollut. Bull.* **2018**, *133*, 442–447. [CrossRef] [PubMed]
75. Wu, Q.; Li, G.; Huo, T.; Du, X.; Yang, Q.; Hung, T.-C.; Yan, W. Mechanisms of parental co-exposure to polystyrene nanoplastics and microcystin-LR aggravated hatching inhibition of zebrafish offspring. *Sci. Total Environ.* **2021**, *774*, 145766. [CrossRef]
76. Naidu, S.A.; Rao, V.R.; Ramu, K. Microplastics in the benthic invertebrates from the coastal waters of Kochi, Southeastern Arabian Sea. *Environ. Geochem. Health* **2018**, *40*, 1377–1383. [CrossRef] [PubMed]
77. Wegner, A.; Besseling, E.; Foekema, E.; Kamermans, P.; Koelmans, A. Effects of nanopolystyrene on the feeding behavior of the blue mussel (*Mytilus edulis* L.). *Environ. Toxicol. Chem.* **2012**, *31*, 2490–2497. [CrossRef] [PubMed]
78. Li, Y.; Wang, J.; Yang, G.; Lu, L.; Zheng, Y.; Zhang, Q.; Zhang, X.; Tian, H.; Wang, W.; Ru, S. Low level of polystyrene mi-croplastics decreases early developmental toxicity of phenanthrene on marine medaka (*Oryzias melastigma*). *J. Hazard. Mater.* **2020**, *385*, 121586. [CrossRef]
79. Daugherty, M. Adsorption of Organic Pollutants to Microplastics: The Effects of Dissolved Organic Matter. Master's Thesis, Northwestern University, Semester in Environmental Science Class of 2016, (Mentors: Conte, M.; Weber, J.C.). Evanston, IL, USA, 2016; pp. 1–27. Available online: https://www.mbl.edu/ses/files/2017/02/Daugherty-Revised-FINAL.pdf (accessed on 1 September 2021).
80. Li, J.; Zhang, K.; Zhang, H. Adsorption of antibiotics on microplastics. *Environ. Pollut.* **2018**, *237*, 460–467. [CrossRef]

81. Sokač, D.G.; Stanić, M.H.; Bušić, V.; Zobundžija, D. Occurrence of pharmaceuticals in surface water. *Croat. J. Food Sci. Technol.* **2017**, *9*, 204–210. [CrossRef]
82. Gassel, M.; Rochman, C.M. The complex issue of chemicals and microplastic pollution: A case study in North Pacific lanternfish. *Environ. Pollut.* **2019**, *248*, 1000–1009. [CrossRef] [PubMed]
83. Kedzierski, M.; D'Almeida, M.; Magueresse, A.; Le Grand, A.; Duval, H.; César, G.; Sire, O.; Bruzaud, S.; Le Tilly, V. Threat of plastic ageing in marine environment. Adsorption/desorption of micropollutants. *Mar. Pollut. Bull.* **2018**, *127*, 684–694. [CrossRef] [PubMed]
84. Amelia, T.S.M.; Khalik, W.M.A.W.M.; Ong, M.C.; Shao, Y.T.; Pan, H.J.; Bhubalan, K. Marine microplastics as vectors of major ocean pollutants and its Hazard.s to the marine ecosystem and humans. *Prog. Earth Planet Sci.* **2021**, *8*, 1–26. [CrossRef]
85. Barboza, L.G.A.; Vethaak, A.D.; Lavorante, B.R.; Lundebye, A.-K.; Guilhermino, L. Marine microplastic debris: An emerging issue for food security, food safety and human health. *Mar. Pollut. Bull.* **2018**, *133*, 336–348. [CrossRef]
86. Batel, A.; Linti, F.; Scherer, M.; Erdinger, L.; Braunbeck, T. Transfer of benzo a pyrene from microplastics to Artemia nauplii and further to zebrafish via a trophic food web experiment: CYP1A induction and visual tracking of persistent organic pollutants. *Environ. Toxicol. Chem.* **2016**, *35*, 1656–1666. [CrossRef] [PubMed]
87. Khan, F.R.; Boyle, D.; Chang, E.; Bury, N.R. Do PE microplastic beads alter the intestinal uptake of Ag in rainbow trout Oncorhynchus mykiss? Analysis of the microplastics vector effect using in vitro gut sacs. *Environ. Pollut.* **2017**, *231*, 200–206. [CrossRef] [PubMed]
88. Kim, D.; Chae, Y.; An, Y.-J. Mixture Toxicity of Nickel and Microplastics with Different Functional Groups on *Daphnia magna*. *Environ. Sci. Technol.* **2017**, *51*, 12852–12858. [CrossRef]
89. Prata, J.C.; Lavorante, B.R.; Montenegro, M.D.C.B.; Guilhermino, L. Influence of microplastics on the toxicity of the pharmaceuticals procainamide and doxycycline on the marine microalgae Tetraselmis chuii. *Aquat. Toxicol.* **2018**, *197*, 143–152. [CrossRef] [PubMed]
90. Syberg, K.; Nielsen, A.; Khan, F.; Banta, G.T.; Palmqvist, A.; Jepsen, P.M. Microplastic potentiates triclosan toxicity to the marine copepod Acartia tonsa (Dana). *J. Toxicol. Environ. Health Part A* **2017**, *80*, 1369–1371. [CrossRef]
91. Gonzalez, N.; Hatfield, J.; Katsumiti, A.; Duroudier, N.; Lacave, J.M.; Bilbao, E.; Orbea, A.; Navarro, E.; Cajaraville, M.P. Impacts of dietary exposure to different sized polystyrene microplastics alone and with sorbed benzo[a]pyrene on biomarkers and whole organism responses in mussels Mytilus galloprovincialis. *Sci. Total Environ.* **2019**, *684*, 548–566. [CrossRef]
92. Tang, Y.; Rong, J.; Guan, X.; Zha, S.; Shi, W.; Han, Y.; Du, X.; Wu, F.; Huang, W.; Liu, G. Immunotoxicity of microplastics and two persistent organic pollutants alone or in combination to a bivalve species. *Environ. Pollut.* **2019**, *258*, 113845. [CrossRef]
93. Magara, G.; Khan, F.R.; Pinti, M.; Syberg, K.; Inzirillo, A.; Elia, A.C. Effects of combined exposures of fluoranthene and polyethylene or polyhydroxybutyrate microplastics on oxidative stress biomarkers in the blue mussel (*Mytilus edulis*). *J. Toxicol. Environ. Health Part A* **2019**, *82*, 616. [CrossRef] [PubMed]
94. Kleinteich, J.; Seidensticker, S.; Marggrander, N.; Zarfl, C. Microplastics Reduce Short-Term Effects of Environmental Contaminants. Part II: Polyethylene Particles Decrease the Effect of Polycyclic Aromatic Hydrocarbons on Microorganisms. *Int. J. Environ. Res. Public Healh* **2018**, *15*, 287. [CrossRef] [PubMed]
95. Pittura, L.; Avio, C.G.; Giuliani, M.E.; D'Errico, G.; Keiter, S.; Cormier, B.; Gorbi, S.; Regoli, F. Microplastics as Vehicles of Environmental PAHs to Marine Organisms: Combined Chemical and Physical Hazard.s to the Mediterranean Mussels, Mytilus galloprovincialis. *Front. Mar. Sci.* **2018**, *5*, 103. [CrossRef]
96. Teixeira, M.; Almeida, Â.; Calisto, V.; Esteves, V.; Schneider, R.J.; Wrona, F.J.; Soares, A.M.; Figueira, E.; Freitas, R. Toxic effects of the antihistamine cetirizine in mussel Mytilus galloprovincialis. *Water Res.* **2017**, *114*, 316–326. [CrossRef] [PubMed]
97. Mezzelani, M.; Gorbi, S.; Regoli, F. Pharmaceuticals in the aquatic environments: Evidence of emerged threat and future challenges for marine organisms. *Mar. Environ. Res.* **2018**, *140*, 41–60. [CrossRef]
98. Almeida, Â.; Calisto, V.; Esteves, V.I.; Schneider, R.J.; Figueira, E.; Soares, A.M.V.M.; Freitas, R. Can ocean warming alter sub-lethal effects of antiepileptic and antihistaminic pharmaceuticals in marine bivalves? *Aquat. Toxicol.* **2021**, *230*, 105673. [CrossRef]
99. Maulvault, A.L.; Santos, L.; Camacho, C.; Anacleto, P.; Barbosa, V.L.; Alves, R.; Ferreira, P.P.; Serra-Compte, A.; Barceló, D.; Rodriguez-Mozaz, S.; et al. Antidepressants in a changing ocean: Venlafaxine uptake and elimination in juvenile fish (*Argyrosomus regius*) exposed to warming and acidification conditions. *Chemosphere* **2018**, *209*, 286–297. [CrossRef]
100. Rodrigues, S.; Antunes, S.; Correia, A.T.; Golovko, O.; Žlábek, V.; Nunes, B. Assessment of toxic effects of the antibiotic erythromycin on the marine fish gilthead seabream (*Sparus aurata* L.) by a multi-biomarker approach. *Chemosphere* **2018**, *216*, 234–247. [CrossRef]
101. McCallum, E.S.; Sundelin, A.; Fick, J.; Alanärä, A.; Klaminder, J.; Hellström, G.; Brodin, T. Investigating tissue bioconcentration and the behavioural effects of two pharmaceutical pollutants on sea trout (*Salmo trutta*) in the laboratory and field. *Aquat. Toxicol.* **2019**, *207*, 170–178. [CrossRef]
102. Zhong, X.; Zhu, Y.; Wang, Y.; Zhao, Q.; Huang, H. Effects of three antibiotics on growth and antioxidant response of *Chlorella pyrenoidosa* and *Anabaena cylindrica*. *Ecotoxicol. Environ. Saf.* **2021**, *211*, 111954. [CrossRef]
103. Matozzo, V.; Battistara, M.; Marisa, I.; Bertin, V.; Orsetti, A. Assessing the effects of amoxicillin on antioxidant enzyme activ-ities, lipid peroxidation and protein carbonyl content in the clam *Ruditapes philippinarum* and the mussel *Mytilus galloprovin-cialis*. *Bull. Environ. Contam. Toxicol.* **2016**, *97*, 521–527. [CrossRef]

104. Matozzo, V.; Bertin, V.; Battistara, M.; Guidolin, A.; Masiero, L.; Marisa, I.; Orsetti, A. Does the antibiotic amoxicillin affect haemocyte parameters in non-target aquatic invertebrates? The clam *Ruditapes philippinarum* and the mussel *Mytilus galloprovincialis* as model organisms. *Mar. Environ. Res.* **2016**, *119*, 51–58. [CrossRef]
105. Trombini, C.; da Fonseca, T.G.; Morais, M.D.B.; Rocha, T.L.; Blasco, J.; Bebianno, M.J. Toxic effects of cisplatin cytostatic drug in mussel *Mytilus galloprovincialis*. *Mar. Environ. Res.* **2016**, *119*, 12–21. [CrossRef]
106. Capolupo, M.; Valbonesi, P.; Kiwan, A.; Buratti, S.; Franzellitti, S.; Fabbri, E. Use of an integrated biomarker-based strategy to evaluate physiological stress responses induced by environmental concentrations of caffeine in the Mediterranean mussel *Mytilus galloprovincialis*. *Sci. Total Environ.* **2016**, *563-564*, 538–548. [CrossRef]
107. Aguirre-Martínez, G.V.; DelValls, T.A.; Martín-Díaz, M.L. General stress, detoxification pathways, neurotoxicity and geno-toxicity evaluated in *Ruditape philippinarum* exposed to human pharmaceuticals. *Ecotoxicol. Environ. Saf.* **2016**, *124*, 18–31. [CrossRef] [PubMed]
108. Fernandes, E.; Fonseca, T.G.; Carriço, T.; Mestre, N.; Tavares, A.; Bebianno, M.J. Cytotoxic responses of the anticancer drug cyclophosphamide in the mussel Mytilus galloprovincialis and comparative sensitivity with human cells lines. *Chemosphere* **2020**, *261*, 127678. [CrossRef] [PubMed]
109. Liang, R.; Shao, X.; Shi, Y.; Jiang, L.; Han, G. Antioxidant defenses and metabolic responses of blue mussels (Mytilus edulis) exposed to various concentrations of erythromycin. *Sci. Total Environ.* **2019**, *698*, 134221. [CrossRef] [PubMed]
110. Freitas, R.; Almeida, Â.; Calisto, V.; Velez, C.; Moreira, A.; Schneider, R.; Esteves, V.; Wrona, F.J.; Figueira, E.; Soares, A.M.V.M. The impacts of pharmaceutical drugs under ocean acidification: New data on single and combined long-term effects of car-bamazepine on *Scrobicularia plana*. *Sci. Total Environ.* **2016**, *541*, 977–985. [CrossRef] [PubMed]
111. Cruz, J.D.; Almeida, A.; Calisto, V.; Esteves, V.I.; Schneider, R.J.; Wrona, F.J.; Soares, A.M.; Figueira, E.; Freitas, R. Caffeine impacts in the clam Ruditapes philippinarum: Alterations on energy reserves, metabolic activity and oxidative stress biomarkers. *Chemosphere* **2016**, *160*, 95–103. [CrossRef] [PubMed]
112. Costa, S.; Coppola, F.; Pretti, C.; Intorre, L.; Meucci, V.; Soares, A.M.; Freitas, R.; Solé, M. The influence of climate change related factors on the response of two clam species to diclofenac. *Ecotoxicol. Environ. Saf.* **2020**, *189*, 109899. [CrossRef]
113. Chen, S.; Shen, Z.; Ding, J.; Qu, M.; Li, T.; Tong, M.; Di, Y. Sulfamethoxazole induced systematic and tissue-specific antioxidant defense in marine mussels (*Mytilus galloprovincialis*): Implication of antibiotic's ecotoxicity. *Chemosphere* **2021**, *279*, 130634. [CrossRef]
114. Serra-Compte, A.; Alvarez-Munoz, D.; Sole, M.; Caceres, N.; Barcelo, D.; Rodríguez- Mozaz, S. Comprehensive study of sulfamethoxazole effects in marine mussels: Bioconcentration, enzymatic activities and metabolomics. *Environ. Res.* **2019**, *173*, 12–22. [CrossRef]
115. Serra-Compte, A.; Maulvault, A.L.; Camacho, C.; Alvarez-Muñoz, D.; Barceló, D.; Rodríguez-Mozaz, S.; Marques, A. Effects of water warming and acidification on bioconcentration, metabolization and depuration of pharmaceuticals and endocrine disrupting compounds in marine mussels (*Mytilus galloprovincialis*). *Environ. Pollut.* **2018**, *236*, 824–834. [CrossRef] [PubMed]
116. Han, Y.; Zhou, W.; Tang, Y.; Shi, W.; Shao, Y.; Ren, P.; Zhang, J.; Xiao, G.; Sun, H.; Liu, G. Microplastics aggravate the bioaccumulation of three veterinary antibiotics in the thick shell mussel *Mytilus coruscus* and induce synergistic immunotoxic effects. *Sci. Total Environ.* **2021**, *770*, 145273. [CrossRef] [PubMed]
117. Pires, A.; Almeida, A.; Correia, J.; Calisto, V.; Schneider, R.J.; Esteves, V.; Soares, A.; Figueira, E.; Freitas, R. Long-term exposure to caffeine and carbamazepine: Impacts on the regenerative capacity of the polychaete *Diopatra neapolitana*. *Chemosphere* **2015**, *146*, 565–573. [CrossRef] [PubMed]
118. Pires, A.; Almeida, A.; Calisto, V.; Schneider, R.J.; Esteves, V.I.; Wrona, F.J.; Soares, A.M.; Figueira, E.; Freitas, R. Long-term exposure of polychaetes to caffeine: Biochemical alterations induced in *Diopatra neapolitana* and *Arenicola marina*. *Environ. Pollut.* **2016**, *214*, 456–463. [CrossRef] [PubMed]
119. Fonseca, T.G.; Morais, M.B.; Rocha, T.; Abessa, D.M.S.; Aureliano, M.; Bebianno, M.J. Ecotoxicological assessment of the an-ticancer drug cisplatin in the polychaete Nereis diversicolor. *Sci. Total Environ.* **2017**, *575*, 162–172. [CrossRef] [PubMed]
120. Fonseca, T.; Auguste, M.; Ribeiro, F.; Cardoso, C.; Mestre, N.; Abessa, D.; Bebianno, M. Environmental relevant levels of the cytotoxic drug cyclophosphamide produce harmful effects in the polychaete *Nereis diversicolor*. *Sci. Total Environ.* **2018**, *636*, 798–809. [CrossRef]
121. Da Fonseca, T.G.; Abessa, D.M.S.; Bebianno, M.J. Effects of mixtures of anticancer drugs in the benthic polychaete Nereis di-versicolor. *Environ. Pollut.* **2019**, *252*, 1180–1192. [CrossRef]
122. Nunes, B.; Leal, C.; Rodrigues, S.; Antunes, S.C. Assessment of ecotoxicological effects of ciprofloxacin in *Daphnia magna*: Life-history traits, biochemical and genotoxic effects. *Water Sci. Technol.* **2018**, *2017*, 835–844. [CrossRef]
123. Ragusa, M.A.; Costa, S.; Cuttitta, A.; Gianguzza, F.; Nicosia, A. Coexposure to sulfamethoxazole and cadmium impairs development and attenuates transcriptional response in sea urchin embryo. *Chemosphere* **2017**, *180*, 275–284. [CrossRef] [PubMed]
124. Almeida, A.; Freitas, R.; Calisto, V.; Esteves, V.; Schneider, R.J.; Soares, A.M.; Figueira, E.; Campos, B.; Barata, C. Effects of carbamazepine and cetirizine under an ocean acidification scenario on the biochemical and transcriptome responses of the clam Ruditapes philippinarum. *Environ. Pollut.* **2018**, *235*, 857–868. [CrossRef]
125. Almeida, A.; Calisto, V.; Esteves, V.; Schneider, R.J.; Soares, A.M.; Figueira, E.; Freitas, R. Effects of single and combined exposure of pharmaceutical drugs (carbamazepine and cetirizine) and a metal (cadmium) on the biochemical responses of R. philippinarum. *Aquat. Toxicol.* **2018**, *198*, 10–19. [CrossRef]

126. Almeida, Â.; Solé, M.; Soares, A.M.; Freitas, R. Anti-inflammatory drugs in the marine environment: Bioconcentration, metabolism and sub-lethal effects in marine bivalves. *Environ. Pollut.* **2020**, *263*, 114442. [CrossRef]
127. Queirós, V.; Azeiteiro, U.M.; Soares, A.M.; Freitas, R. The antineoplastic drugs cyclophosphamide and cisplatin in the aquatic environment—Review. *J. Hazard. Mater.* **2021**, *412*, 125028. [CrossRef]
128. Sachaniya, B.; Gosai, H.; Panseriya, H.; Vala, A.; Dave, B. Polycyclic Aromatic Hydrocarbons (PAHs): Occurrence and Bioremediation in the Marine Environment. In *Marine Pollution: Current Status, Impacts and Remedies*; Bentham Science Publishers Pte: Singapore, 2019; Volume 1, pp. 435–466.
129. Pan, L.; Xu, R.; Wen, J.; Guo, R. Assessing PAHs pollution in Shandong coastal area (China) by combination of chemical analysis and responses of reproductive toxicity in crab Portunus trituberculatus. *Environ. Sci. Pollut. Res.* **2017**, *24*, 14291–14303. [CrossRef] [PubMed]
130. An, S.-A.; Hong, S.; Lee, J.; Cha, J.; Lee, S.; Moon, H.-B.; Giesy, J.P.; Khim, J.S. Identification of potential toxicants in sediments from an industrialized area in Pohang, South Korea: Application of a cell viability assay of microalgae using flow cytometry. *J. Hazard. Mater.* **2020**, *405*, 124230. [CrossRef] [PubMed]
131. Ben Garali, S.M.; Sahraoui, I.; Ben Othman, H.; Kouki, A.; de la Iglesia, P.; Diogène, J.; Lafabrie, C.; Andree, K.B.; Fernández-Tejedor, M.; Mejri, K.; et al. Capacity of the potentially toxic diatoms Pseudo-nitzschia mannii and Pseudo-nitzschia hasleana to tolerate polycyclic aromatic hydrocarbons. *Ecotoxicol. Environ. Saf.* **2021**, *214*, 112082. [CrossRef]
132. Duran, R.; Cravo-Laureau, C. Role of environmental factors and microorganisms in determining the fate of polycyclic aromatic hydrocarbons in the marine environment. *FEMS Microbiol. Rev.* **2016**, *40*, 814–830. [CrossRef] [PubMed]
133. Renegar, D.A.; Turner, N.R. Species sensitivity assessment of five Atlantic scleractinian coral species to 1-methylnaphthalene. *Sci. Rep.* **2021**, *11*, 1–17. [CrossRef]
134. Hwang, K.; Lee, J.; Kwon, I.; Park, S.Y.; Yoon, S.J.; Lee, J.; Kim, B.; Kim, T.; Kwon, B.-O.; Hong, S.; et al. Large-scale sediment toxicity assessment over the 15,000 km of coastline in the Yellow and Bohai seas, East Asia. *Sci. Total Environ.* **2021**, *792*, 148371. [CrossRef]
135. Cong, Y.; Wang, Y.; Zhang, M.; Jin, F.; Mu, J.; Li, Z.; Wang, J. Lethal, behavioral, growth and developmental toxicities of al-kyl-PAHs and non-alkyl PAHs to early-life stage of brine shrimp, *Artemia parthenogenetica*. *Ecotoxicol. Environ. Saf.* **2021**, *220*, 112302. [CrossRef]
136. Yang, Y.; Pan, L.; Zhou, Y.; Xu, R.; Miao, J.; Gao, Z.; Li, D. Damages to biological macromolecules in gonadal subcellular fractions of scallop Chlamys farreri following benzo[a]pyrene exposure: Contribution to inhibiting gonadal development and reducing fertility. *Environ. Pollut.* **2021**, *283*, 117084. [CrossRef]
137. Thor, P.; Granberg, M.E.; Winnes, H.; Magnusson, K. Severe Toxic Effects on Pelagic Copepods from Maritime Exhaust Gas Scrubber Effluents. *Environ. Sci. Technol.* **2021**, *55*, 5826–5835. [CrossRef] [PubMed]
138. Wise, C.F.; Wise, J.T.F.; Wise, S.S.; Wise, J.P., Sr. Chemically dispersed oil is cytotoxic and genotoxic to sperm whale skin cells. *Comp. Biochem. Physiol. C: Toxicol. Pharmacol.* **2018**, *208*, 64–70. [CrossRef] [PubMed]
139. Costa, E.; Piazza, V.; Gambardella, C.; Moresco, R.; Prato, E.; Biandolino, F.; Cassin, D.; Botter, M.; Maurizio, D.; D'Adamo, R.; et al. Ecotoxicological effects of sediments from Mar Piccolo, South Italy: Toxicity testing with organisms from different trophic levels. *Environ. Sci. Pollut. Res.* **2015**, *23*, 12755–12769. [CrossRef]
140. Liu, F.; Tu, T.; Li, S.; Cai, M.; Huang, X.; Zheng, F. Relationship between plankton-based β-carotene and biodegradable adaptability to petroleum-derived hydrocarbon. *Chemosphere* **2019**, *237*, 124430. [CrossRef]
141. Bretherton, L.; Hillhouse, J.; Kamalanathan, M.; Finkel, Z.V.; Irwin, A.J.; Quigg, A. Trait-dependent variability of the response of marine phytoplankton to oil and dispersant exposure. *Mar. Pollut. Bull.* **2020**, *153*, 110906. [CrossRef]
142. Niehus, N.C.; Floeter, C.; Hollert, H.; Witt, G. Miniaturised Marine Algae Test with Polycyclic Aromatic Hydrocarbons−Comparing Equilibrium Passive Dosing and Nominal Spiking. *Aquat. Toxicol.* **2018**, *198*, 190–197. [CrossRef] [PubMed]
143. Ben Othman, H.; Lanouguère, E.; Got, P.; Hlaili, A.S.; Leboulanger, C. Structural and functional responses of coastal marine phytoplankton communities to PAH mixtures. *Chemosphere* **2018**, *209*, 908–919. [CrossRef] [PubMed]
144. Ben Othman, H.; Pringault, O.; Louati, H.; Hlaili, A.S.; Leboulanger, C. Impact of contaminated sediment elutriate on coastal phytoplankton community (Thau lagoon, Mediterranean Sea, France). *J. Exp. Mar. Biol. Ecol.* **2017**, *486*, 1–12. [CrossRef]
145. Sakka Hlaili, A.; Sahraoui, I.; Bouchouicha-Smida, D.; Melliti Ben Garali, S.; Ksouri, J.; Chalghaf, M.; Bates, S.S.; Lundholm, N.; Kooistra, W.H.C.; de la Iglesia, P.; et al. Toxic and potentially toxic diatom blooms in Tunisian (SW Mediterranean) waters: Review of ten years of investigations. In *Advances in Environmental Research*; Daniels, J.A., Ed.; Nova Publisher: New York, NY, USA, 2016; Volume 48, pp. 51–70.
146. Honda, M.; Suzuki, N. Toxicities of Polycyclic Aromatic Hydrocarbons for Aquatic Animals. *Int. J. Environ. Res. Public Health* **2020**, *17*, 1363. [CrossRef]
147. Romero, I.C.; Sutton, T.; Carr, B.; Quintana-Rizzo, E.; Ross, S.W.; Hollander, D.J.; Torres, J.J. Decadal Assessment of Polycyclic Aromatic Hydrocarbons in Mesopelagic Fishes from the Gulf of Mexico Reveals Exposure to Oil-Derived Sources. *Environ. Sci. Technol.* **2018**, *52*, 10985–10996. [CrossRef] [PubMed]
148. Incardona, J.P.; Scholz, N. The influence of heart developmental anatomy on cardiotoxicity-based adverse outcome pathways in fish. *Aquat. Toxicol.* **2016**, *177*, 515–525. [CrossRef]

149. Magnuson, J.T.; Khursigara, A.J.; Allmon, E.B.; Esbaugh, A.J.; Roberts, A.P. Effects of Deepwater Horizon crude oil on ocular development in two estuarine fish species, red drum (*Sciaenops ocellatus*) and sheepshead minnow (*Cyprinodon variegatus*). *Ecotoxicol. Environ. Saf.* **2018**, *166*, 186–191. [CrossRef] [PubMed]
150. Cherr, G.N.; Fairbairn, E.; Whitehead, A. Impacts of Petroleum-Derived Pollutants on Fish Development. *Annu. Rev. Anim. Biosci.* **2017**, *5*, 185–203. [CrossRef]
151. Idowu, O.; Semple, K.; Ramadass, K.; O'Connor, W.; Hansbro, P.; Thavamani, P. Beyond the obvious: Environmental health implications of polar polycyclic aromatic hydrocarbons. *Environ. Int.* **2019**, *123*, 543–557. [CrossRef]
152. Sørensen, L.; Sørhus, E.; Nordtug, T.; Incardona, J.P.; Linbo, T.L.; Giovanetti, L.; Karlsen, Ø.; Meier, S. Oil droplet fouling and differential toxicokinetics of polycyclic aromatic hydrocarbons in embryos of Atlantic haddock and cod. *PLoS ONE* **2017**, *12*, e0180048. [CrossRef]
153. Colli-Dula, R.C.; Fang, X.; Moraga-Amador, D.; Albornoz-Abud, N.; Zamora-Bustillos, R.; Conesa, A.; Zapata-Perez, O.; Moreno, D.; Hernandez-Nuñez, E. Transcriptome analysis reveals novel insights into the response of low-dose benzo(a)pyrene exposure in male tilapia. *Aquat. Toxicol.* **2018**, *201*, 162–173. [CrossRef] [PubMed]
154. Ikegame, M.; Hattori, A.; Tabata, M.J.; Kitamura, K.; Tabuchi, Y.; Furusawa, Y.; Maruyama, Y.; Yamamoto, T.; Sekiguchi, T.; Matsuoka, R.; et al. Melatonin is a potential drug for the prevention of bone loss during space flight. *J. Pineal Res.* **2019**, *67*, e12594. [CrossRef] [PubMed]
155. Frapiccini, E.; Annibaldi, A.; Betti, M.; Polidori, P.; Truzzi, C.; Marini, M. Polycyclic aromatic hydrocarbon (PAH) accumulation in different common sole (*Solea solea*) tissues from the North Adriatic Sea peculiar impacted area. *Mar. Pollut. Bull.* **2018**, *137*, 61–68. [CrossRef]
156. Ranjbar Jafarabadi, A.; Riyahi Bakhtiari, A.; Yaghoobi, Z.; Kong Yap, C.; Maisano, M.; Cappello, T. Distributions and compositional patterns of polycyclic aromatic hydrocarbons (PAHs) and their derivatives in three edible fishes from Kharg coral Island, Persian Gulf, Iran. *Chemosphere* **2019**, *215*, 835–845. [CrossRef] [PubMed]
157. Yu, F.; Yang, C.; Zhu, Z.; Bai, X.; Ma, J. Adsorption behavior of organic pollutants and metals on micro/nanoplastics in the aquatic environment. *Sci. Total Environ.* **2019**, *694*, 133643. [CrossRef] [PubMed]
158. Soltani, N.; Moore, F.; Keshavarzi, B.; Sorooshian, A.; Javid, R. Potentially toxic elements (PTEs) and polycyclic aromatic hy-drocarbons (PAHs) in fish and prawn in the Persian Gulf, Iran. *Ecotoxicol. Environ. Saf.* **2019**, *173*, 251–265. [CrossRef] [PubMed]
159. Honda, M.; Qiu, X.; Koyama, J.; Uno, S.; Undap, S.L.; Shimasaki, Y.; Oshima, Y. The Wharf Roach, *Ligia* sp., A Novel Indicator of Polycyclic Aromatic Hydrocarbon Contamination in Coastal Areas. *Int. J. Environ. Res.* **2017**, *12*, 1–11. [CrossRef]
160. Ghaeni, M.; Pour, N.A.; Hosseini, M. Bioaccumulation of polychlorinated biphenyl (PCB), polycyclic aromatic hydrocarbon (PAH), mercury, methyl mercury, and arsenic in blue crab Portunus segnis from Persian Gulf. *Environ. Monit. Assess.* **2015**, *187*, 1–9. [CrossRef]
161. Ruberg, E.J.; Williams, T.D.; Elliott, J.E. Review of petroleum toxicity in marine reptiles. *Ecotoxicology* **2021**, *30*, 525–536. [CrossRef] [PubMed]
162. Milton, S.; Lutz, P.; Shigenaka, G. Oil toxicity and impacts on sea turtles. In *Oil and Sea Turtles: Biology, Planning, and Response*; Shigenaka, G., Ed.; NOAA, National Ocean Service, Office of Response and Restoration: Seattle, WA, USA, 2003; pp. 35–48.
163. Mitchelmore, C.L.; Bishop, C.A.; Collier, T.K. Toxicological estimation of mortality of oceanic sea turtles oiled during the Deepwater Horizon oil spill. *Endanger. Species Res.* **2017**, *33*, 39–50. [CrossRef]
164. Stacy, N.; Field, C.L.; Staggs, L.; MacLean, R.A.; Stacy, B.A.; Keene, J.; Cacela, D.; Pelton, C.; Cray, C.; Kelley, M.; et al. Clinicopathological findings in sea turtles assessed during the Deepwater Horizon oil spill response. *Endanger. Species Res.* **2017**, *33*, 25–37. [CrossRef]
165. Harms, C.A.; McClellan-Green, P.; Godfrey, M.H.; Christiansen, E.F.; Broadhurst, H.J.; Godard-Codding, C.A.J. Crude Oil and Dispersant Cause Acute Clinicopathological Abnormalities in Hatchling Loggerhead Sea Turtles (*Caretta caretta*). *Front. Vet. Sci.* **2019**, *6*, 344. [CrossRef]
166. Kocmoud, A.R.; Wang, H.-H.; Grant, W.E.; Gallaway, B.J. Population dynamics of the endangered Kemp's ridley sea turtle following the 2010 oil spill in the Gulf of Mexico: Simulation of potential cause-effect relationships. *Ecol. Model.* **2018**, *392*, 159–178. [CrossRef]
167. Frasier, K.E.; Solsona-Berga, A.; Stokes, L.; Hildebrand, J.A. Impacts of the deepwater horizon oil spill on marine mammals and sea turtles. In *Deep Oil Spills*; Murawski, S., Ed.; Springer: Cham, Switzerland, 2020; pp. 431–462.
168. Ylitalo, G.M.; Collier, T.K.; Anulacion, B.F.; Juaire, K.; Boyer, R.H.; Da Silva, D.A.M.; Keene, J.L.; Stacy, B.A. Determining oil and dispersant exposure in sea turtles from the northern Gulf of Mexico resulting from the Deepwater Horizon oil spill. *Endanger. Species Res.* **2017**, *33*, 9–24. [CrossRef]
169. Ruberg, E.J.; Elliott, J.E.; Williams, T.D. Review of petroleum toxicity and identifying common endpoints for future research on diluted bitumen toxicity in marine mammals. *Ecotoxicology* **2021**, *30*, 537–551. [CrossRef]
170. Smith, C.R.; Rowles, T.K.; Hart, L.B.; Hart, L.B.; Townsend, F.I.; Wells, R.S.; Zolman, E.S.; Balmer, B.C.; Quigley, B.; Ivančić, M.; et al. Slow recovery of Barataria Bay dolphin health following the Deepwater Horizon oil spill (2013–2014), with evidence of persistent lung disease and impaired stress response. *Endanger. Species Res.* **2017**, *33*, 127–142. [CrossRef]

171. De Guise, S.; Levin, M.; Gebhard, E.; Jasperse, L.; Hart, L.B.; Smith, C.R.; Venn-Watson, S.; Townsend, F.; Wells, R.; Balmer, B.; et al. Changes in immune functions in bottlenose dolphins in the northern Gulf of Mexico associated with the Deepwater Horizon oil spill. *Endanger. Species Res.* **2017**, *33*, 291–303. [CrossRef]
172. White, N.D.; Godard-Codding, C.; Webb, S.J.; Bossart, G.D.; Patricia, A.; Fair, P.A. Immunotoxic effects of in vitro exposure of dolphin lymphocytes to Louisiana sweet crude oil and CorexitTM. *J. Appl. Toxicol.* **2017**, *37*, 676–682. [CrossRef]
173. Kellar, N.M.; Speakman, T.R.; Smith, C.R.; Lane, S.M.; Balmer, B.C.; Trego, M.L.; Catelani, K.N.; Robbins, M.N.; Allen, C.D.; Wells, R.S.; et al. Low reproductive success rates of common bottlenose dolphins *Tursiops truncatus* in the northern Gulf of Mexico following the Deepwater Horizon disaster (2010–2015). *Endanger. Species Res.* **2017**, *33*, 143–158. [CrossRef]
174. Wilkin, S.; Rowles, T.; Stratton, E.; Adimey, N.; Field, C.; Wissmann, S.; Shigenaka, G.; Fougères, E.; Mase, B.; Stranding, N.S.R.; et al. Marine mammal response operations during the Deepwater Horizon oil spill. *Endanger. Species Res.* **2017**, *33*, 107–118. [CrossRef]
175. Olguín-Jacobson, C.; Pitt, K.; Carroll, A.R.; Melvin, S.D. Polyps of the Jellyfish Aurelia aurita Are Unaffected by Chronic Exposure to a Combination of Pesticides. *Environ. Toxicol. Chem.* **2020**, *39*, 1685–1692. [CrossRef]
176. WHO. *WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification*, 2019 ed.; World Health Organization: Geneva, Switzerland, 2020.
177. Olsvik, P.A.; Larsen, A.K.; Berntssen, M.H.G.; Goksøyr, A.; Karlsen, O.A.; Yadetie, F.; Sanden, M.; Kristensen, T. Effects of Agricultural Pesticides in Aquafeeds on Wild Fish Feeding on Leftover Pellets Near Fish Farms. *Front. Genet.* **2019**, *10*, 794. [CrossRef]
178. Thomas, M.C.; Flores, F.; Kaserzon, S.; Fisher, R.; Negri, A.P. Toxicity of ten herbicides to the tropical marine microalgae Rhodomonas salina. *Sci. Rep.* **2020**, *10*, 7612–7616. [CrossRef] [PubMed]
179. De Carvalho, R.C.; Feijão, E.; Matos, A.R.; Cabrita, M.T.; Novais, S.C.; Lemos, M.F.L.; Caçador, I.; Marques, J.C.; Reis-Santos, P.; Fonseca, V.F.; et al. Glyphosate-Based Herbicide Toxicophenomics in Marine Diatoms: Impacts on Primary Production and Physiological Fitness. *Appl. Sci.* **2020**, *10*, 7391. [CrossRef]
180. Thomas, M.C.; Flores, F.; Kaserzon, S.; Reeks, T.A.; Negri, A.P. Toxicity of the herbicides diuron, propazine, tebuthiuron, and haloxyfop to the diatom *Chaetoceros muelleri*. *Sci. Rep.* **2020**, *10*, 1–14. [CrossRef]
181. Howe, P.L.; Reichelt-Brushett, A.J.; Clark, M.W.; Seery, C.R. Toxicity estimates for diuron and atrazine for the tropical marine cnidarian *Exaiptasia pallida* and in-hospite *Symbiodinium* spp. using PAM chlorophyll-a fluorometry. *J. Photochem. Photobiol. B Biol.* **2017**, *171*, 125–132. [CrossRef]
182. Rowen, D.J.; Templeman, M.; Kingsford, M. Herbicide effects on the growth and photosynthetic efficiency of *Cassiopea maremetens*. *Chemosphere* **2017**, *182*, 143–148. [CrossRef]
183. Asnicar, D.; Cappelli, C.; Sallehuddin, A.S.; Maznan, N.A.; Marin, M.G. Effects of Glyphosate-Based and Derived Products on Sea Urchin Larval Development. *J. Mar. Sci. Eng.* **2020**, *8*, 661. [CrossRef]
184. Bringer, A.; Thomas, H.; Prunier, G.; Dubillot, E.; Clérandeau, C.; Pageaud, M.; Cachot, J. Toxicity and risk assessment of six widely used pesticides on embryo-larval development of the Pacific oyster, *Crassostrea gigas*. *Sci. Total Environ.* **2021**, *779*, 146343. [CrossRef]
185. Brain, R.; Anderson, J.; Hanson, M. Acute and early life-stage toxicity of atrazine in sheepshead minnow (*Cyprinodon variegatus*). *Ecotoxicol. Environ. Saf.* **2021**, *218*, 112303. [CrossRef] [PubMed]
186. Deidda, I.; Russo, R.; Bonaventura, R.; Costa, C.; Zito, F.; Lampiasi, N. Neurotoxicity in Marine Invertebrates: An Update. *Biology* **2021**, *10*, 161. [CrossRef] [PubMed]
187. Richardson, J.R.; Fitsanakis, V.; Westerink, R.H.S.; Kanthasamy, A. Neurotoxicity of pesticides. *Acta Neuropathol.* **2019**, *138*, 343–362. [CrossRef] [PubMed]
188. Sylwestrzak, Z.; Zgrundo, A.; Pniewski, F. Ecotoxicological Studies on the Effect of Roundup® (Glyphosate Formulation) on Marine Benthic Microalgae. *Int. J. Environ. Res. Public Health* **2021**, *18*, 884. [CrossRef]
189. Strachan, F.; Kennedy, C.J. The environmental fate and effects of anti-sea lice chemotherapeutants used in salmon aquaculture. *Aquaculture* **2021**, *544*, 737079. [CrossRef]
190. Yu, H.; Peng, J.; Cao, X.; Wang, Y.; Zhang, Z.; Xu, Y.; Qi, W. Effects of microplastics and glyphosate on growth rate, morphological plasticity, photosynthesis, and oxidative stress in the aquatic species *Salvinia cucullate*. *Environ. Pollut.* **2021**, *279*, 116900. [CrossRef]
191. Moeris, S.; Vanryckeghem, F.; Demeestere, K.; De Schamphelaere, K.A. Neonicotinoid Insecticides from a Marine Perspective: Acute and Chronic Copepod Testing and Derivation of Environmental Quality Standards. *Environ. Toxicol. Chem.* **2021**, *40*, 1353–1367. [CrossRef] [PubMed]
192. Yamamura, Y.; Takeda, K.; Kawai, Y.K.; Ikenaka, Y.; Kitayama, C.; Kondo, S.; Kezuka, C.; Taniguchi, M.; Ishizuka, M.; Nakayama, S.M. Sensitivity of turtles to anticoagulant rodenticides: Risk assessment for green sea turtles (*Chelonia mydas*) in the Ogasawara Islands and comparison of warfarin sensitivity among turtle species. *Aquat. Toxicol.* **2021**, *233*, 105792. [CrossRef] [PubMed]
193. Kim, H.; Wang, H.; Ki, J.-S. Chloroacetanilides inhibit photosynthesis and disrupt the thylakoid membranes of the dinoflagellate Prorocentrum minimum as revealed with metazachlor treatment. *Ecotoxicol. Environ. Saf.* **2021**, *211*, 111928. [CrossRef] [PubMed]
194. El Ayari, T.; Mhadhbi, L.; Dabara, N.; Znati, M.; Dab, H. The detoxifying effect of Polygonum equisetiforme extracts against dichlorvos (DDVP)-induced oxidative stress and neurotoxicity in the commercial clam *Ruditapes decussatus*. *Environ. Sci. Pollut. Res. Int.* **2020**, *27*, 10449–10458. [CrossRef]

195. Gambardella, C.; Nichino, D.; Iacometti, C.; Ferrando, S.; Falugi, C.; Faimali, M. Long term exposure to low dose neurotoxic pesticides affects hatching, viability and cholinesterase activity of Artemia spp. *Aquat. Toxicol.* **2018**, *196*, 79–89. [CrossRef]
196. Juhel, G.; Bayen, S.; Goh, C.; Lee, W.K.; Kelly, B.C. Use of a suite of biomarkers to assess the effects of carbamazepine, bisphenol A, atrazine, and their mixtures on green mussels, *Perna viridis*. *Environ. Toxicol. Chem.* **2016**, *36*, 429–441. [CrossRef]
197. Zhang, X.; Li, S.; Wang, C.; Tian, H.; Wang, W.; Ru, S. Effects of monocrotophos pesticide on cholinergic and dopaminergic neurotransmitter systems during early development in the sea urchin *Hemicentrotus pulcherrimus*. *Toxicol. Appl. Pharmacol.* **2017**, *328*, 46–53. [CrossRef] [PubMed]
198. Duarte-Restrepo, E.; Jaramillo-Colorado, B.E.; Duarte-Jaramillo, L. Effects of chlorpyrifos on the crustacean *Litopenaeus van-namei*. *PLoS ONE* **2020**, *15*, 0231310.
199. Pinteus, S.; Lemos, M.F.L.; Freitas, R.; Duarte, I.M.; Alves, C.; Silva, J.; Marques, S.C.; Pedrosa, R. Medusa polyps ad-herence inhibition: A novel experimental model for antifouling assays. *Sci. Total Environ.* **2020**, *715*, 136796. [CrossRef]
200. Jung, S.; Bae, J.; Kang, S.; Son, J.; Jeon, J.; Lee, H.; Sidharthan, M.; Ryu, S.; Shin, H. Acute toxicity of organic antifouling biocides to phytoplankton *Nitzschia pungens* and zooplankton *Artemia larvae*. *Mar. Pollut. Bull.* **2017**, *124*, 811–818. [CrossRef]
201. Avelelas, F.; Martins, R.; Oliveira, T.; Maia, F.; Malheiro, E.; Soares, A.; Loureiro, S.; Tedim, J. Efficacy and Ecotoxicity of Novel Anti-Fouling Nanomaterials in Target and Non-Target Marine Species. *Mar. Biotechnol.* **2017**, *19*, 164–174. [CrossRef] [PubMed]
202. Gutner-Hoch, E.; Martins, R.; Oliveira, T.; Maia, F.; Soares, A.M.V.M.; Loureiro, S.; Piller, C.; Preiss, I.; Weis, M.; Larroze, S.B.; et al. Antimacrofouling Efficacy of Innovative Inorganic Nanomaterials Loaded with Booster Biocides. *J. Mar. Sci. Eng.* **2018**, *6*, 6. [CrossRef]
203. Wendt, I.; Backhaus, T.; Blanck, H.; Arrhenius, A. The toxicity of the three antifouling biocides DCOIT, TPBP and medetomidine to the marine pelagic copepod *Acartia tonsa*. *Ecotoxicology* **2016**, *25*, 871–879. [CrossRef] [PubMed]
204. Hano, T.; Ohkubo, N.; Mochida, K. A hepatic metabolomics-based diagnostic approach to assess lethal toxicity of dithiocar-bamate fungicide polycarbamate in three marine fish species. *Ecotoxicol. Environ. Saf.* **2017**, *138*, 64–70. [CrossRef] [PubMed]