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Review

Implications for the seafood industry, consumers and the environment arising from contamination of shellfish with pharmaceuticals, plastics and potentially toxic elements: A case study from Irish waters with a global orientation

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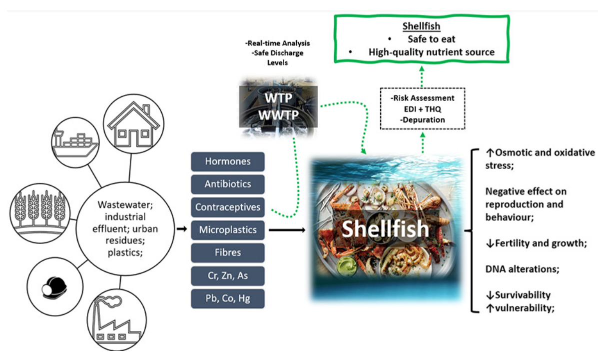
HIGHLIGHTS

- Increased presence of pharmaceuticals, plastics and potentially toxic elements in shellfish waters
- Potential implications for industry and consumers arising from contaminated seafood
- Main contaminants and pressure points are reviewed offering potential solutions.
- Need for increased stakeholder awareness along with commensurate risk mitigation
- Risk assessment to safeguard shellfish industry and to protect food supply chain

GRAPHICAL ABSTRACT



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ABSTRACT

Shellfish are a rich source of minerals, B-vitamins and omega-3 to the human diet. The global population is expected to reach 9.6 billion people by 2050 where there will be increased demand for shellfish and for sustained improvements in harvesting. The production of most consumed species of shellfish is sea-based and are thus susceptible to *in situ* environmental conditions and water quality. Population growth has contributed to expansion of urbanization and the generation of effluent and waste that reaches aquatic environments, potentially contaminating seafood by exposure to non-treated effluents or inappropriately discarded waste. Environmental contaminants as microplastics (MP), pharmaceuticals (PHAR) and potentially toxic contaminants (PTE) are being identified in all trophic levels and are a current threat to both shellfish and consumer safety. Immunotoxicity, genotoxicity, fertility reduction, mortality and bioaccumulation of PTE are representative examples of the variety of effects already established in contaminated shellfish. In humans, the consumption of contaminated shellfish can lead to neurological and developmental effects, reproductive and gastrointestinal disorders and in extreme cases, death. This timely review provides insights into the presence of MP, PHAR and PTE in shellfish, and estimate the daily intake and hazard quotient for consumption behaviours. Alternatives approaches for seafood depuration that encompass risk reduction are addressed, to reflect state of the art knowledge from a Republic of Ireland perspective. Review of best-published literature revealed that

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MP, PHAR and PTE contaminants were detected in commercialised species of shellfish, such as *Crassostrea* and *Mytilus*. The ability to accumulate these contaminants by shellfish due to feeding characteristics is attested by extensive *in vitro* studies. However, there is lack of knowledge surrounding the distribution of these contaminants in the aquatic environment their interactions with humans. Preventive approaches including risk assessment are necessary to safeguard the shellfish industry and the consumer.

Contents

1. Introduction

Shellfish are aquatic invertebrates that have been used as a source of food by humans for over 160,000 years — and were one of the last additions to the human diet before the revolutionary culture of plants and domestication of animals (Marean et al., 2007). Shellfish can be classified as crustaceans or molluscs. There are approximately 40,000 known species of crustaceans, characterized by a segmented body protected by a hard shell, as observed in well-known species such as shrimp, crabs and lobsters (Hobbs, 2012; Prié, 2019). In the molluscs group, around 85,000 species such as slugs, snails, mussels, clams and octopuses, are grouped by distinctive characteristics including a muscular foot, and a fleshy mantle covering the viscera (Hobbs, 2012).

The importance of shellfish to the human diet and the rising demand for shellfish products has led to the development of production systems to increase availability and support harvesting from natural sources. In 2012, aquaculture (fish, shellfish, aquatic plants and molluscs) surpassed wild catches and production increased by 250 % between 2000 and 2015 (FAO, 2016; Hannah and Max, 2021). In 2018, global seafood production reached 179 million metric tons. Shellfish are a rich source of nutrients for the human diet. Benefits include the presence of a wide variety of essential amino acids, B-vitamins, and minerals in relatively high concentrations. They are an important source of omega-3,6 fatty acids, high levels of easily digestible protein, have low levels of fat and calories, and contain nutraceuticals with antioxidant, antiobesity, antidiabetes, and immunomodulatory activities (Venugopal and Gopakumar, 2017). However, the presence of contaminants in water and production plant systems can lead to harmful effects and illnesses, including disruptions in the human endocrine system, and immuno-genotoxicity in shellfish (Álvarez-Muñoz et al., 2015; Gadelha et al., 2019; Lacaze et al., 2015).

Most shellfish are cultivated in sea-based systems which rely on good water quality and environmental conditions. Geographical information, water quality reports from monitoring programs and risk modelling are important resources in the selection of appropriate sites for shellfish farms (Silva et al., 2011). Nonetheless, the discharge of industrial, domestic and agricultural effluents are unpredictable factors and result in chemical pollution, including pharmaceuticals, pesticides, metabolites, organic compounds and personal care products (Fairbairn et al., 2016). The growing population and agricultural demand for food has increased the use of pesticides and the discharge of domestic effluents, which also contaminate the seafood industry (Gadelha et al., 2019).

There is a constant requirement to remove persistent pharmaceuticals (PHAR) from the effluent matrix, including stimulants, anti-inflammatories, antibiotics and many other drugs (Hernando et al., 2006). If not removed, these PHAR will end up in the environment, reaching the shellfish and ultimately being consumed through the human diet. Potentially toxic elements (PTE) are naturally present in the environment at non-hazardous concentrations. However, these elements have been detected in toxic levels in industrialized areas such as ports, areas with mining activity, post-environmental accidents, as well as in discharge of effluent into rivers and seas (Bayen et al., 2005). The persistence and high accumulative potential of PTE have been extensively detected in a wide variety of shellfish species (Wang et al., 2018). The intensive use of plastics and poor management of waste have also contributed to their dispersal in terrestrial and aquatic environments. Nowadays, plastic materials and microplastics (MP) can be found in the seabed and riverbed, suspended in water or deposited at coastal areas; studies have also demonstrated MP translocation to the circulatory system in mussels (Browne et al., 2008; Hantoro et al., 2019).

The interactions of the shellfish industry and environmental conditions are not only evident through contamination and pollution issues — but shellfish farms must also deal with the uncertainty arising from climate change. Ocean acidification and changing temperature are examples of processes that can impact plankton levels and shellfish metabolism, leading to complete decimation of cultures (Froehlich et al., 2018). The physiological effects of temperature and contamination on to the bivalve *M. arenaria* were reported by Greco et al. (2011). Increased temperature altered the response to a mixture of herbicides, enhancing the malondialdehyde content, cytochrome C oxidase and superoxide dismutase activity. Shellfish farms must also deal with natural predators, and the challenge of protecting the shellfish without affecting the ecological balance (Rheault, 2012). The survivability of shellfish farms is essential as a source of food and protection of wild stocks, and the dependence on a healthy environment for shellfish production stimulates the protection of cultured areas. Understanding the risks associated with shellfish production is the first step towards ensuring food safety and quality, therefore, a risk assessment (RA) strategy can represent an important resource to support the identification of risks, effects, and development of preventive strategies. The long coastline of Ireland, together with its importance as a marine habitat to many finfish and shellfish species, implies the need for new studies in preservation and protection. The Irish Marine Institute, an Irish state agency, has been providing essential monitoring of a wide range of contaminants in Irish waters. These studies were reviewed with available literature to diagnose the current situation in Ireland.

The objective of this review paper is to discuss the presence, in shellfish, of PHA, PTE and MP that represent a threat to the host and human safety, with insights into contaminants present in Irish waters, and state of the art. The regulations for maximum limits will be discussed in a way as to be used as a guide for researchers and for the shellfish farming industry. This paper will also address the concept and main steps involved in implementing a risk assessment to support the development of protective strategies, and also a guide to estimate the ingestion of contaminants and hazard quotient based on consumption profile and contaminant concentration.

2. Pharmaceuticals in shellfish

The rate of increase of available medicines to treat and assist society is remarkable. Nonetheless, a wide variety of compounds produced for medical purposes have been identified as contaminants in different environments (Alygizakis et al., 2016; Mezzelani et al., 2018). The low degradation rate and high persistence of pharmaceutical (PHAR) compounds under environmental conditions represents a risk to aquatic environments, wildlife, and human safety (Almeida et al., 2020). Wastewater treatment plants are able to partially reduce the levels of PHAR from domestic effluent, however, the constant discharges and inadequate disposal methods increase their abundance in the environment, reaching aquatic organisms through the food chain, from phytoplankton, bivalves and crustaceans, to fish (Álvarez-Muñoz et al., 2015; Jjemba, 2018). The environmental concentration of PHAR in the marine environment can be found at ng L^{-1} to μg L^{-1} levels, and can lead to sub-lethal or chronic toxicity, while higher concentrations induce acute effects on reproduction and development (Capolupo et al., 2018; Fabbri and Franzellitti, 2016). When absorbed, PHAR compounds can lead to alterations in DNA, gene expression, antioxidant activity and immune responses, reflecting negatively on growth, behaviour and reproduction (Almeida et al., 2020; Lacaze et al., 2015).

Tiedeken et al. (2017) reported that pollution of European receiving waters with PHAR, such as with 17-beta-estradiol (a natural estrogenic hormone, E2), along with the pharmaceutically-active compounds diclofenac (an anti-inflammatory drug, DCL) and 17-alpha-ethynylestradiol (a synthetic estrogenic hormone, EE2) is a ubiquitous phenomenon. These authors noted that European surface water concentrations of DCL are typically reported below the proposed annual average environmental quality standard (AA EQS) of 100 ng L^{-1}, but that exceedances frequently occur. E2 and EE2 surface water concentrations are typically below 50 ng L^{-1} and 10 ng L^{-1} respectively, but these values greatly exceed the proposed AA EQS values for these compounds (0.04 and 0.035 ng L^{-1} respectively). Levels of these PHARs are frequently reported to be disproportionately high in EU receiving waters, particularly in effluents at control points that require urgent attention. Overall, it was found that DCL and EE2 enter European aquatic environments mainly following human consumption and excretion of therapeutic drugs, and by incomplete removal from influent at urban wastewater treatment plants (WWTPs) (Tiedeken et al., 2017). E2 is a natural hormone excreted by humans, which also experiences incomplete removal during WWTPs treatment (Tahar et al., 2018). Current conventional analytical chemistry methods are sufficiently sensitive for the detection and quantification of DCL, but not for E2 and EE2, thus alternative, ultra-trace, time-integrated monitoring techniques such as passive sampling are needed to inform water quality for these estrogens (Tiedeken et al., 2017). DCL appears resistant to conventional wastewater treatment while E2 and EE2 have high removal efficiencies that occur through biodegradation or sorption to organic matter (Tahar et al., 2018).

The presence of PHAR in Irish surface waters has been reported by McEneff et al. (2014). Carbamazepine, diclofenac, gemfibrozil, mefenamic acid and trimetrophim were found in >85 % of the samples collected from two exposure sites in the West and East of Ireland, and two areas close to effluent treatment stations. These drugs were also detected at slightly lower concentrations in the marine surface water and can be accumulated in the shellfish, as observed for the marine mussels.

Beyond the importance highlighted by consumption, molluscs, especially bivalves, have also been used as bioindicators of pollution since they exhibit the required characteristics to evaluate an environment: they are filter feeders, show bioaccumulation, have a wide distribution, exhibit slow movement and have well-characterized life-cycles (Almeida et al., 2020; McEneff et al., 2014). Capolupo et al. (2018) address this characteristic by reporting the impact of contraceptive PHAR on molluscs in a study of *in vitro* inhibition of mussel (*Mytilus galloprovincialis*) gamete fertilization induced by 500 ng L^{-1} of contraceptive 17-α ethinylestradiol (EE2), and also a reduction of fertility in sea urchins (*Paracentrotus lividus*) at 5000 ng L^{-1} of the lipid regulator gemfibrozil. Analyses of exposure during early phases are required to evaluate the effects of contaminants on animal development. EE2 and other active substances such as flame retardants, pesticides and fungicides are also considered emergent pollutants due to their endocrine-disruptive activity (Álvarez-Muñoz et al., 2015; Fehrenbach et al., 2021). Purdom et al. (1994) first registered the feminisation of male fish after exposure to treated effluent water, identifying the female hormone vitellogenin, naturally produced by the liver in females under use of estrogens. The occurrence of endocrine-disrupting compounds (EDC) is associated with human presence, and not restricted to contaminated areas or effluent discharges. As reported by Álvarez-Muñoz et al. (2015), in a study of 19 EDCs, 10 were present in bivalves and/or fish from the Tagus estuary (Portugal), Scheldt estuary (Netherlands), Po delta (Italy) and Ebro delta (Spain). The highest level of an EDC was observed in mullet, a fish found worldwide, containing 98.4 ng g^{-1} dw of flame retardant Tris(2-butoxyethyl) phosphate. Chiu et al. (2018) deployed the native mussels *M. galloprovincialis*, *M. coruscus* and *P. viridis* and semipermeable membrane devices in highly industrialized coastal areas to assess the presence of EDCs. In one month of exposure, the concentration of EDCs ranged from 99.4 to 326 ng g^{-1} dw and a correlation between the membranes and mussels was observed, confirming the potential of shellfish as indicators due to filter feeding ability.

In vitro studies with blue mussel (*Mytilus edulis*) using the psychotropic drugs paroxetine and venlafaxine at 1.5 μg L^{-1}, generated DNA breaks in hemocytes, and caused immunomodulation, respectively; the antibiotic trimethoprim was genotoxic at 200 μg L^{-1} and immunotoxic at 20 μg L^{-1}, and the same effects were reported for erythromycin at concentrations higher than 20 μg L^{-1} (Lacaze et al., 2015). The ability of the organism to retain the tested compounds, together with high consumption of blue mussel worldwide, reveal the risk of consuming this filter feeder produced/caught in contaminated environments. The presence of pharmaceuticals (PHAR) in the marine environment occurs uninterrupted (Capolupo et al., 2018), as demonstrated by Álvarez-Muñoz et al. (2015) with the identification of 15 out of 23 tested PHAR in *Mytilus* spp., *Chamalea gallina* and *Crassostrea gigas* collected in Portugal, Italy and Spain. The same authors identified 10 EDCs out of 20 compounds analysed in the mullet (*L. aurata*) and flounder (*P. flesus*) in Portugal and the Netherlands, respectively. On the Arabian Sea coast, the exposure to polycyclic aromatic hydrocarbons (PAH) and potentially toxic elements available in the water has induced DNA damage in the oyster *Sacccostrea cucullate* (Sarker et al., 2018).

The wide variety of drugs present in different environments and shellfish species, and their effects, are described in Table 1.

PHARs can complex with organic compounds present in complex matrices as wastewater, resulting in higher persistence and accumulation in receiving waters. Wastewater treatment plants (WWTP) are responsible for reducing the impact of urban and industrial effluent through the removal of nutrients and contaminants. Mechanical, chemical, physical and biological processes are applied in the preliminary, primary, secondary and tertiary treatment steps (McEneff et al., 2015). PHAR are mostly removed in the tertiary treatment by biodegradation with adapted and capable bacteria in bioreactor and/or physical and mechanical as filtration and ozonation. Angeles et al. (2020) reported >95 % overall removal for 14 out of 11 PHAR compounds detected in WWTP, while biological treatment provided negative to <50 %. Higher removal efficiencies employing physical and mechanical as filtration are usually associated to increased treatment costs and maintenance.

Tahar et al. (2018) reported that of approximately 1000 WWTPs in the Republic of Ireland, only 16 have been monitored for PHARs. Diclofenac is

Table 1
Pharmaceuticals and respective drugs detected in shellfish, marine water or tested in *in vitro* studies. The main effects observed are addressed with the duration of exposure.

Drug	Concentration and exposure time	Species	Environment or assay	Effect	Ref.
EE2	5 and 50 ng L^{-1}; 39 d	*M. edulis*	Marine	Reproductive system	(Blalock et al., 2018)
	5 to 425 ng L^{-1}; 20 h	*C. gigas*	Marine	Embryotoxicity	(Wessel et al., 2007)
	1 μg L^{-1}; 10 exp + 8 dep	*C. virginica*	Marine	Osmotic and oxidative stress, bioconcentration, metabolism	(Brew et al., 2020)
	5 ng L^{-1}; 12 d	*E. complanata*	Freshwater	Reproductive behaviour and biochemical parameters	(Leonard et al., 2017)
	5, 50 and 500 ng L^{-1}; 48 to 96 h	*M. galloprovincialis*, *P. lividus* and *S. aurata*	*In vitro*	Alteration in gamete fertilization and morphological abnormalities in *M. galloprovincialis* and *P. lividus*. Decreased survival of *S. aurata*.	(Capolupo et al., 2018)
IBP	1 and 100 μg L^{-1}; 7 d	*C. gigas*	*In vitro*	Increased transcription of certain genes and alterations in auxiliary enzymes and antioxidants	(Serrano et al., 2015)
	0.1 to 50 μg L^{-1}; 14 d	*R. philippinarum*	*In vitro*	Decrease in lysosomal membrane stability; induced detoxification metabolism and oxidative stress; genotoxic effects	(Aguirre-Martínez et al., 2016)
	15 ng g^{-1}; 48 h	*P. perna*	Marine sediment	Development affected; decrease in lysosomal membrane stability	
DCF	100 and 600 μg L^{-1}; 7 d	*M. galloprovincialis*	*In vitro*	Identification of 13 metabolites from DCF spiking	(Bonnefille et al., 2017)
	2.5 μg L^{-1}; 60 d	*M. galloprovincialis*	*In vitro*	IBU and KTP presented the same effects as DCF. Genotoxic, modulation of lipid metabolism, alterations of immunological parameters, and changes in cellular turn-over	(Mezzelani et al., 2018)
	0.5 μg L^{-1}; 96 h	*R. philippinarum*	*In vitro* flow through system	Mortality increases for larvae, shell alterations, increase in lactase activity	(Munari et al., 2016)
PAR	0.5, 5, 50 and 500 μg L^{-1}; 96 h	*Mytilus* spp.	*In vitro*	Reduce of food intake, increase in glycogen levels, metabolic changes	(Piedade et al., 2020)
	40, 250 and 100 μg L^{-1}; 7 d	*M. edulis*	*In vitro*	Alterations in gene expression affecting the reproductive system	(Koagouw and Ciocan, 2020)
	1 and 100 μg L^{-1}; 1, 4 and 7 d	*C. gigas*	*In vitro*	Alterations at transcriptional level	(Bebianno et al., 2017)
PROP	500, 5000 and 50,000 ng L^{-1}; 48 to 96 h	*M. galloprovincialis,* and *S. aurata*	*In vitro*	Fertilization and survival reduction in *P. lividus* and morphological abnormalities in *M. galloprovincialis*	(Capolupo et al., 2018)
TCS	75 ng g^{-1}; 24 h	*L. variegatus*; *M. charruana*	Marine sediment	Development affected; decrease in lysosomal membrane stability	(Pusceddu et al., 2018)
	0.007, 0.014, and 0.036 mg L^{-1}; 20 d	*C. catla*	*In vitro*	Enhanced GOT, GPT, and GST enzyme activity; physiological alterations	(Hemalatha et al., 2019)

EE2: 17alpha-ethinylestradiol; IBP: ibuprofen; DCF: diclofenac; KTP: ketoprofen; PAR: paracetamol; PROP: propranolol; TCS: triclosan; GOT: glutamate oxaloacetate transaminase; GPT: glutamate pyruvate transaminase; GST: glutathione-S-transferase; dep: depuration; exp: exposure.

found in treated effluents from 5 WWTPs at levels at least as high as other European WWPTs, and sometimes higher. Measurements of E2 and EE2 in WWPT effluents were rare and effluents were more often evaluated for total estrogens; these PHARs were generally not detected using conventional analytical methods because of limits of detection being too high compared to environmental concentrations and WFD environmental quality standards (Tiedeken et al., 2017; Tahar et al., 2018). Tahar et al. (2018) reported a correlation between occurrence of these PHAR and regional drug dispensing data in Ireland. However, mapping the aforementioned data onto appropriate river basin catchment management tools will inform predictive and simulated risk determinations to inform investment in infrastructure that is necessary to protect rivers and beaches and economic activities that rely on clean water.

Adams et al. (2002) spiked sterile river water with common antibiotics to evaluate the effectiveness of conventional water treatment processes on antibiotic removal. They reported an effective removal when applying chlorine, ozone, powdered activated carbon and reverse osmosis, however, only powdered activated carbon (PAC) effectively removed the antibiotics at typical plant dosages of PAC and at a frequency that increases the treatment costs. However, matrices with higher concentrations of PHAR, such as urban wastewater, can make removal of PHAR more challenging. In shellfish, (McEneff et al., 2013) investigated the concentration of PHAR after a cooking process, spiking *Mytilus* spp. and artificial seawater with several PHAR at concentrations 1000 times greater than those observed in marine surface waters. The authors observed an increase of pharmaceutical residues in seawater and shellfish tissue after cooking by steaming. Currently, there is no standard method for PHAR removal in shellfish and seawater, as this depends on several parameters. The continuous water quality monitoring at shellfish farms and surroundings is essential to monitor the PHAR level. An early detection can reduce the bioconcentration and possibly the natural depuration of contaminants in controlled conditions.

3. Plastics and microplastics in shellfish

Plastics are polymeric materials of highly diverse composition and uses, moulded under specific pressure and temperature to provide adequate resistance and performance (FAO, 2018). The demand for plastic materials has been constantly increasing over the past decades and reached a worldwide production of 368 million tonnes in 2019 (PlasticsEurope, 2020). The intensive usage of plastic materials and inadequate management to control its life cycle have led to dispersal in the terrestrial and aquatic environments, expanding to shorelines, open ocean and reaching the deep seas. It has been estimated that between 4.8 and 12.7 million tons of plastic entered the oceans in 2010, not including abandoned equipment and fishing nets (Jambeck et al., 2015). Contamination occurs on different levels, where low-density plastics are dominant and float at the top layers, and high-density plastics combined with biofouled low-density material sink and remain on the sea bottom (Andrady, 2011; Bellas et al., 2016). The physical properties of plastic materials, such as resistance, durability, light weight, and generally low cost make them appropriate for use in ropes, cages, tanks and general materials associated with the fish and shellfish industry. However, this can also threaten shellfish and finfish safety as these materials are not completely inert, where degradation under environmental conditions such as ultraviolet radiation and/or physical abrasion can release plastic fibres and particles in even higher concentrations than external contaminants (Hantoro et al., 2019).

The ingestion of plastic materials occurs involuntarily in finfish and shellfish; however, filter feeders are more susceptible to accumulating higher concentration of plastics than finfish due to non-selective feeding. Plastics can reach shellfish directly as primary plastic of specific size and composition, or as secondary materials of different sizes and composition, products of exposure to environmental conditions and ultraviolet radiation (Hantoro et al., 2019). The secondary plastics are mostly present as fibres, powders, and pellets, classified by size as meso (>5 mm), micro (1000 nm) and nanoplastics (1–100 nm). In invertebrates, once the microplastic is ingested it can be transferred to body tissues though the gut epithelial lining or egested in faeces (Browne et al., 2008). To investigate the presence of plastic materials in the oyster *C. gigas* and mussel *M. edulis*, van Cauwenberghe et al. (2015) performed an overnight digestion of shellfish wet tissue using nitric acid (69 %) followed by a boiling step, where samples from a mussel farm and local supermarket resulted in 0.36 and 0.47 particles/g of tissue, respectively. Using the same digestion protocol, van Cauwenberghe and Janssen (2014) detected microplastics (MP) in all animal tissues and faeces collected from *M. edulis* and *A. marina* and an increase of energy consumption in the exposed *M. edulis* when compared to control, linked to increase of stress. Browne et al. (2008) used *M. edulis* as a model organism to investigate the route and biological consequences of ingesting microparticles of polystyrene, a polymer that reached a worldwide production of 15.61 million metric tons in 2021 (Statista, 2020). They identified a correlation between smaller particles and high accumulation in tissues. In 3 days, particles moved from the gut to the circulatory system and remained for 48 h, reaching their greatest level on the 12th day. Ingested microplastics can also work as a carrier of other contaminants to seafood and not only a direct contaminant. Polychlorinated biphenyls and bacteria were reported on polystyrene surface of eight of the 14 species analysed by Carpenter et al. (1972).

The accidental ingestion of plastics due to similarity to food can be summed up with the contamination of lower trophic levels and subsequent trophic transfer, as observed by the same authors in zooplankton samples. Crustaceans, for example, are non-selective and can have a wide variety of food sources. This fact might explain the presence of microplastics in the gastrointestinal tract of the crustacean *Nephrops norvegicus*, collected in Irish prawn grounds and presented by Hara et al. (2020). Fibres were predominant (98 % of plastic constituent) in the collected plastic and a positive correlation was observed between the prawn carapace condition and microplastic. Devriese et al. (2015) reported the natural ability for the shrimp *Crangon crangon* to ingest microplastics, reaching an uptake of 0.68 g w w^{-1}. The role of shrimps in the trophic transfer of microplastics was also discussed as the variable diet of shrimps and the importance as food for a large range of predators contributes to transfer.

On the Irish continental shelf, an extension from the coastline of 200 nautical miles under the sea, microplastics were detected within superficial sediments and bottom water (Martin et al., 2017). The depth and environmental conditions at these regions slow the breakdown of plastic materials, contributing to their persistence and accumulation. Woodall et al. (2014) reports the high concentration of microplastics in samples collected from the North Atlantic Ocean, Mediterranean Sea and SW Indian Ocean. Microplastics were mostly in the form of fibres of 2–3 mm in length and <0.1 mm in diameter in deep-sea sediments and coral samples, regions widely habited by commercially explored finfish and shellfish. Lusher et al. (2018) reported the presence of macro-debris and micro-debris in Irish cetaceans, which shows trophic transfer as another route of contamination. The authors also observed a higher incidence of macrodebris ingestion in deep-diving species, however, it was not possible to investigate the relationship to habitat. Ireland is not located in accumulation zone of debris, however due to an extension of 7524 km, a combination of weather, season and geographical position can lead to high accumulation levels (Lusher et al., 2018). Concentration of microplastics such as fibres, fragments, films and filaments detected in shellfish species at different locations are presented in Table 2.

An alternative for reducing the levels of plastic in shellfish is a longer depuration process keeping the shellfish in tanks with recirculating water that pass through a treatment system, allowing the excretion of plastic materials from the gut. Depuration processes are designed to provide optimum conditions such as temperature, salinity and oxygenation, reducing the impact on organoleptic properties and increasing the filtering activity. van Cauwenberghe and Janssen (2014) reported a reduction in the levels of particles in *M. edulis* and *C. gigas* after depurating for three days. Alternatively, a change in the mode of consumption can be made by removing parts of the shellfish or cooking. However, this can impact on consumer experience and affect important characteristics to shellfish as freshness. Daniel et al. (2020) suggested the consumption of *F. indicus* in whole dried by cooking or peeled form to reduce the exposure to microplastics owing to the concentration in the foregut and midgut. However, more studies are needed to improve the depuration and cleaning processes while preserving the organoleptic properties.

4. Potentially toxic elements in shellfish

Potentially toxic elements (PTE) are pollutants of high persistence and toxicity that contaminate a wide variety of ecosystems and organisms (Wang et al., 2018). The term PTE describes metals and metalloids that naturally present in soil, and some are considered essential nutrients, required at low doses and participating in biochemical and physiological functions (Tchounwou et al., 2012). Others, such as lead, mercury, and cadmium, are on a list of ten chemicals of major public concern (World Health Organization, 2020a). Anthropogenic activities such as general industrial processes, mining, agriculture, and domestic use of PTE have been associated with environmental contamination and human exposure (Tchounwou et al., 2012). Marine and freshwater ecosystems are highly affected by PTE, where shellfish can accumulate these compounds to toxic concentrations, releasing them back into the water after death, or transporting them to the next trophic level (Djedjibegovic et al., 2020). The ability of shellfish species to bioaccumulate chemicals, their long-life span, and high density, have supported their use as local bioindicators of contamination, where the determination of PTE is determined directly from the shellfish tissue (El-Shenawy et al., 2016).

The most common method to verify the presence of metals in shellfish is by total concentration, extracting all the contaminants from tissues and analysing by specialized techniques; they can also be determined in terms of bioacessibility, which represents the fraction of contaminants that is

Table 2
Concentration of microplastics in shellfish species and major findings.

Microplastic	Concentration	Specie	Comments	Location	Reference
Fibres, fragments and films	1.75 ± 2.01 items per shrimp	*N. norvegicus*	Most common range of 1 to 2 mm	Irish waters	(Hara et al., 2020)
Filaments	83 % contained plastic filaments	*N. norvegicus*	Fishing waste was probably the source for microfilaments	Clyde Sea	(Murray and Cowie, 2011)
Fibres	0.68 ± 0.55 microplastics/g ww	*C. crangon*	The analysed specie was able to ingest plastic particles from natural habitat	Southern North Sea and Channel area	(Devriese et al., 2015)
Microplastics	0.2 ± 0.3 microplastics/g; 1.2 ± 2.8 particles/g	*M. edulis*; *A. marina* (annelid)	Microplastics were present in all organisms collected in the field	French, Belgian and Dutch North Sea coast	(van Cauwenberghe et al., 2015)
Microplastics (LDP, HDP and POS)	0.36 ± 0.07 particles/g (ww); plastic load 0.47 ± 0.16 particles/g ww	*M. edulis*; *C. gigas*	Annual dietary exposure of 11,000 microplastics	North Sea and Atlantic Ocean	(van Cauwenberghe and Janssen, 2014)
Microplastics	128 microplastics (83 % were fibres)	*F. indicus*	Contamination significantly higher in Monsoon season	Coastal waters off Cochin, India	(Daniel et al., 2020)

g: gram; ww: wet weight;

Table 3
Potentially toxic elements quantified in shellfish and seawater. General comments were added to address the main findings of studies.

Metal	Concentration	Specie	Comments	Reference
Cd	2.0–12.4 μg g^{-1} dw	*C. angulate* oysters	Bio-accessibility from 13 to 58 %	(He et al., 2016)
	1.7–5.1 μg^{-1} g	*C. hongkongensis*		
	0.644 mg kg^{-1} ww	*D. gahi*	TWI would be reached in a 70 kg adult by a weekly consumption of 274 g of *M. edulis* or 272 g of *D. gahi*	(Djedjibegovic et al., 2020)
	0.015	*P. monodon*		
	0.002	*P. indicus*		
	0.062	*M. edulis*		
	0.17/0.1/0.135 μg g^{-1} ww	*R. decussatus*	Concentration in three different locations in the Lake Timsah; PTWI: 0.01–0.06 μg kg^{-1}/day) - below the PTWI of 7 μg kg^{-1}/week for both groups of consumers	(El-Shenawy et al., 2016)
	0.23/0.23/0.23	*P. undulate*		
	0.635 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.41 mg kg^{-1} dw	*O. glomerate*	Concentration in seawater 0.08 mg kg^{-1} dw	(Yuan et al., 2020)
	0.31	*P. viridis*		
	0.07	*C. scripta*		
	0.06	*M. edulis*		
	1.14	*G. divaricatum*		
	0.66	*B. virescens*		
	0.03–0.14 mg kg^{-1} ww	Blue mussels	Exceeded the 1881/2006/EC max limit in oyster	(Irish Marine Institute, 2018)
	0.02	Clams		
	0.09–1.25	Oysters (Pacific and native)		
Cu	173–2212 μg g^{-1} dw	*C. angulate oysters*	Bio-accessibility from 42 to 95 %	(He et al., 2016)
	1063–5314 μg g^{-1}	*C. hongkongensis*		
	32.2 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	12.04 mg kg^{-1} dw	*O. glomerate*	Concentration in the seawater 1.48 mg kg^{-1} dw	(Yuan et al., 2020)
	1.58	*P. viridis*		
	0.9	*C. scripta*		
	1.49	*M. edulis*		
	1.1	*G. divaricatum*		
	1.32	*B. virescens*		
	2.53/3.79/3.16 μg g^{-1} ww	*R. decussatus*	Concentration in three different locations in the Lake Timsah; EDI was lower than the FAO/WHO guidelines, meaning that is safe for consumption;	(El-Shenawy et al., 2016)
	2.26/2.64/2.45	*P. undulate*		
	0.38–1.32 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	0.77	Clams		
	1.81–22.2	Oysters (Pacific and native)		
Zn	1173–6050 μg g^{-1} dw	*C. angulate* oysters	Bio-accessibility from 13 to 58 %	(He et al., 2016)
	2103–7021 μg g^{-1}	*C. hongkongensis*		
	154.29 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	10.59 mg kg^{-1} dw	*O. glomerate*	Concentration in the seawater 12.25 mg kg^{-1} dw	(Yuan et al., 2020)
	11.95	*P. viridis*		
	9.79	*C. scripta*		
	10.36	*M. edulis*		
	10.64	*G. divaricatum*		
	11.32	*B. virescens*		
	9.87–21 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	11.4	Clams		
	91.8–448	Oysters (Pacific and native)		
Hg	0.02 mg kg^{-1} ww	*D. gahi*		(Djedjibegovic et al., 2020)
	0.044	*M. edulis*		
	0.058	*P. monodon*		
	0.037	*P. indicus*		
	0.01 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.02 mg kg^{-1} dw	*O. glomerate*	Concentration in seawater 0.007 mg kg^{-1} dw	(Yuan et al., 2020)
	0.02	*P. viridis*		
	0.02	*C. scripta*		
	0.01	*M. edulis*		
	0.02	*G. divaricatum*		
	0.03	*B. virescens*		
	0.01–0.03 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	0.01	Clams		
	0.01–0.04	Oysters (Pacific and native)		
Pb	0.003 mg kg^{-1} ww	*D. gahi*	TWI would be reached in a 70 kg adult by a weekly consumption of 274 g of *M. edulis* or 272 g of *D. gahi*	(Djedjibegovic et al., 2020)
	0.014	*P. monodon*		
	0.013	*P. indicus*		
	0.161	*M. edulis*		
	0.47 mg kg^{-1} dw	*O. glomerate*	Concentration in seawater 0.77 mg kg^{-1} dw	(Yuan et al., 2020)
	0.48	*P. viridis*		
	0.34	*C. scripta*		
	0.44	*M. edulis*		
	0.24	*G. divaricatum*		
	0.83	*B. virescens*		
	0.23 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.05–0.37 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	0.11	Clams		
	0.02–0.13	Oysters (Pacific and native)		
Cr	0.16 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.76 mg kg^{-1} dw	*O. glomerate*	Concentration in seawater 0.72 mg kg^{-1} dw	(Yuan et al., 2020)
	0.78	*P. viridis*		

Table 3 (*continued*)

Metal	Concentration	Specie	Comments	Reference
	1.79	*C. scripta*		
	1.08	*M. edulis*		
	0.78	*G. divaricatum*		
	0.23	*B. virescens*		
	0.08–0.35 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	0.07	Clams		
	0.04–0.9	Oysters (Pacific and native)		
Ni	0.26 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.94/0.9/0.92 μg g^{-1} ww	*R. decussatus*	Concentration in three different locations in the Lake Timsah; EDI between 0.01 and 1.26 μg kg^{-1}/day for both bivalves	(El-Shenawy et al., 2016)
	1.04/1.1/1.07	*P. undulate*		
	0.08–0.26 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	0.05	Clams		
	0.03–0.1	Oysters (Pacific and native)		
As	1.27 mg kg^{-1} ww	Bivalve molluscs		(Wang et al., 2018)
	0.48 mg kg^{-1} dw	*O. glomerate*	Concentration in seawater 0.77 mg kg^{-1} dw	(Yuan et al., 2020)
	0.50	*P. viridis*		
	0.29	*C. scripta*		
	0.22	*M. edulis*		
	0.50	*G. divaricatum*		
	0.39	*B. virescens*		
	1.03–1.82 mg kg^{-1} ww	Blue mussels		(Irish Marine Institute, 2018)
	1.65	Clams		
	1.12–2.69	Oysters (Pacific and native)		

ww: wet weight; dw: dry weight.

released from the food matrix and interacts with the human digestive tract (Brandon et al., 2006; He et al., 2016). Quantification by analytical techniques can be diverse. Wang et al. (2018) applied atomic absorption spectrophotometry to measure Cd, Pb, Cr, Ni, Cu, Zn, and atomic fluorescence spectrophotometry for Hg and As, while Djedjibegovic et al. (2020) analysed Cd and Pb by graphite furnace atomic absorption spectrometry and Hg by flow-injection cold vapour atomic absorption spectrometry. *In vitro* models can also be used to provide analysis of specific routes of consumption such as ingestion and sucking. As an example, He et al. (2016) investigated the bio-accessibility of Cd, Cu and Zn in *Crassostrea angulate* (green oyster) and *Crassostrea hongkongensis* (blue oyster). The oysters were collected from a station along the Jiulong River Estuary, China, and digested by an *in vitro* process that mimics the mouth, stomach and small intestine of humans. The total concentration was higher than maximum levels established by USEPA, and the bioacessibility range from 13 to 95 % highlighted the potential threat to human health and safety. The authors also found a correlation between the shellfish tissue colour and concentration of Cu, Cd and Zn.

The main exposure routes of humans to PTE occurs by ingestion of contaminated food and water. Due to their resistance to relatively polluted environments, shellfish species can bioaccumulate and biomagnify PTE through the food chain. PTE toxic effects are associated with gastrointestinal and kidney dysfunction, vascular damage, birth effects, bloody diarrhoea, and many other disorders (Balali-Mood et al., 2021). When exposed to low PTE doses, the effects can be more complicated to diagnose and correlate with source of intake after a long period of exposure. Mazumdar et al. (2011) found that lead exposure in childhood predicts intellectual function in young adulthood. Therefore, a long-term diet containing low doses can be a silent threat. In shellfish, the exposure to low doses of PTE can lead to incorporation of Pb and Zn instead of Ca, as they are incorporated by the same pathways. Stewart et al. (2021) recently reported the correlation between the weakening of shell strength in *Pecten maximus* and metal pollution in sediments, increasing the vulnerability of the bivalve in the environment.

In Irish Coastal Waters, the levels of PTE in waters and shellfish have been monitored mainly by state agencies such as the Irish Marine Institute (Ireland), and the Centre for Environment, Fisheries and Aquaculture (United Kingdom). A review of the contaminant status of the Irish Sea was reported by Kenny et al. (2005). This 100,000 km^2 area is bounded by Scotland, England, Wales and Ireland. In dredged samples collected from 1995 to 2005, zinc, lead and arsenic were present at higher concentrations than other PTE such as Cu, Ni and Cr. A variation of PTE levels was also observed, allowing the researchers to associate the presence of these chemicals in the environment as a consequence of society, industry and weather particularities. In mussel samples collected from inshore sites of the Irish Sea between 1999 and 2001, the authors also identified levels of Cd (208–465.69 μg kg^{-1} wet weight), Cu (923–1987 μg kg^{-1} wet weight), Pb (352–1668 μg kg^{-1} wet weight), Zn (12,673–37,527 μg kg^{-1} wet weight), Hg (18–70 μg kg^{-1} wet weight) and Ag (50–260 μg kg^{-1} wet weight). The concentrations were below the maximum acceptable limits. Another study by the Irish Marine Institute (2018) quantified several metals in bivalve molluscs collected in the Irish seawater in 2015 — from oysters, blue mussels and clams; only Cd in oysters was above the maximum limit established by 1881/2006/EC. The determination was also carried in seawater and the levels of metals complied with the maximum limits established by the Statutory Instruments and Shellfish Waters Directive. However, the presence of these elements at non-natural levels alerts to an intoxication risk as the accumulation of PTE will depend on consumption habits and local body weight, discussed in the risk assessment.

In Table 3 are presented the main potentially toxic elements and their respective concentrations in shellfish tissues, seawater and after *in situ* studies, during bioacessibility and toxicology assays.

Han et al. (1993) reported one of the first depuration studies of metals in shellfish. *C. gigas* and *M. smarangdium* were collected from a region contaminated with copper and zinc and transferred to natural clean seawater for depuration. A 351 μg g^{-1} day^{-1} depuration rate of cooper was reported for the first 6 days, approximately 67 % of the total in *C. gigas*, and only 36 % of accumulated zinc. Longer depuration periods are associate with increased costs of treatment and infrastructure. FAO (2008) describes the fundamentals and practical aspects of bivalve depuration. A minimum depuration period of 42 h is determined and extended according to contamination/removal levels.

Anacleto et al. (2015) evaluated the effect of depuration process on the levels of S, Cl, K, Ca, Fe, Zn, Br, Cu, Se, Rb and Sr in the bivalves *R. philippinarum*, *M. galloprovincialis*, and *S. plana*, collected at different sites of Tagus estuary. Depuration was performed in recirculating tanks set according to European Guidelines (European Commission, 2004). The level of toxic elements (Hg, Cd, Pb and As) after depuration were reduced in *R. philippinarum* (Hg, Cd, Pb and As), *M. galloprovincialis* (Pb) and *S. plana* (Pb).

Currently, there is no consensus about mitigation methods for removing/reducing PTE in shellfish. More studies are necessary to address effective technologies and factors associated with reduction and quality. The continuous monitoring of PTE levels in the full shellfish farming environment is still the main recommendation.

5. Regulation and international guidelines

In order to protect consumer health and ensure product quality, international commissions have elaborated guidelines and limits for a wide diversity of contaminants. These limits were established to balance the potential benefit of consuming food with even a low concentration of contaminants that would not lead to serious effects, and also to keep the production/depuration costs affordable. European Commission Regulations and the U.S. Food and Drug Administration are the main references for maximum levels of contaminants (Table 4). The limits established by each regulatory agency also set the tolerance for legal actions such as recall of products from the market, shut down of production plants, and fines.

6. Risk assessment and management for addressing contamination in shellfish

The analysis of risks associated with an activity, or a hazard is a holistic approach involving all available knowledge and data that can support a prediction mode (Tahar et al., 2017). Besides the diversity of approaches, the risk assessment (RA) modelling is based on the main steps of hazard identification, exposure assessment, and hazard characterization, resulting in a broad risk characterization (Oscar, 2012; Tiedeken et al., 2017). RA can be applied to different environments, also delineating critical control points along the production and supply chain for industry — every stage of processing, production, storage, marketing and consumption is considered in an industrial environment.

Table 4
Environmental chemical contaminants and tolerable levels allowed in shellfish according to international agencies.

Substance	Group/species	Maximum level (concentration of contaminant per wet weight)
European Commission Regulation[1]		
Lead	Crustaceans	0.5 mg kg^{-1}
	Bivalve molluscs	1.5 mg kg^{-1}
	Cephalopods	0.3 mg kg^{-1}
Cadmium	Bivalve molluscs	1 mg kg^{-1}
	Crustaceans	0.5 mg kg^{-1}
	Cephalopods	1 mg kg^{-1}
Mercury	Crustaceans	0.5 mg kg^{-1}
Dioxins and PCBS	Crustaceans	3.5 pg/g (sum of dioxins), 6.6 (sum of dioxins anddioxin-like PCBs); 75 ng g^{-1} (PCB28, PCB52, PCB101, PCB138, PCB153 and PCB180)
Benzo(*a*)pyrene, benzo(*a*)anthracene, benzo(*b*) fluoranthene and chrysene	Smoked crustaceans	2.0 μg kg^{-1}
	Smoked bivalve molluscs	6 μg kg^{-1} Benzo(*a*)pyrene, 35 μg kg^{-1} Sum of benzo(a)-pyrene, benz(*a*)anthracene, benzo(*b*) fluoranthene and chrysene)
U. S. Food and Drug Administration[2]		
Aldrin/Dieldrin	Shellfish and finfish	0.3 ppm
Chlordane	Shellfish and finfish	0.3 ppm
Chlordecone	Shellfish and finfish	0.3 ppm
	Crabmeat	0.4 ppm
DDT, TDE, DDE	Shellfish and finfish	5 ppm
Heptachlor/Heptachlor Epoxide	Shellfish and finfish	0.3 ppm
Mirex	Shellfish and finfish	0.1 ppm
Arsenic	Crustacea	76 ppm
	Molluscan bivalves	86 ppm
Cadmium	Crustacea	3 ppm
	Molluscan bivalves	4 ppm
Chromium	Crustacea	12 ppm
	Molluscan bivalves	13 ppm
Lead	Crustacea	1.5 ppm
	Molluscan bivalves	1.7 ppm
Nickel	Crustacea	70 ppm
	Molluscan bivalves	80 ppm
Methyl Mercury	Shellfish and finfish	1 ppm
Diquat	Shellfish and finfish	0.1 ppm
Fluridone	Crayfish	0.5 ppm
Glyphosate	Shellfish	3 ppm
PCBs	Shellfish and finfish	2 ppm
2,4-D	Shellfish and finfish	1 ppm
Chinese National Food Safety Standard Maximum Levels of Contaminants in Foods[3]		
Lead	Fish, crustacean	0.5 mg kg^{-1}
	Bivalves	1.5 mg kg^{-1}
Cadmium	Crustacean	0.5
	Bivalves, gastropods, cephalopods, echinoderms	2 (viscera removed)
Methyl mercury	Aquatic animals	0.5 mg kg^{-1}
As	Aquatic animals and its products, not including fish	0.5 mg kg^{-1}
Cr	Aquatic animal and its products	2 mg kg^{-1}
Benzo(*a*)pyrene	Aquatic animals and its products	5 μg kg^{-1}
N-Nitrosodimethylamine	Aquatic animals and its products	4 μg kg^{-1}
Polychlorinated biphenyl	Aquatic animals and its products	0.5 mg kg^{-1}[a]

[1] European Comission Regulation (ECR, 2006).
[2] U.S Food and Drug Administration (USDA, 1996a, 1996b, 1993).
[3] Chinese National Food Safety Standard Maximum Levels of Contaminants in Foods (NHFPC and CFDA, 2017).
[a] Polychlorinated biphenyl is calculated by total of PCB28, PCB52, PCB101, PCB118, PCB138, PCB153 and PCB180.

In the food safety area, RA is based on standard protocols established by governmental and international agencies, focused on standard methods and contaminants limits. However, Tahar et al. (2017) highlighted that developing and deploying an RA model for evaluating environmental threat posed by emerging contaminants of concern is challenging given the multiplicity of influencing and controlling factors to be addressed. The authors defined a semi-quantitative RA model that adopted the Irish EPA's Source-Pathway-Receptor concept to define relevant parameters for calculating low, medium or high-risk scores for each agglomeration of WWTP, which included catchment, treatments, operational and management factors. This RA model may be potentially applied on a transnational scale to (i) identify WWTPs that pose a particular risk as regards releasing disproportionally high levels of contaminants that may reach shellfish, and (ii) to identify priority locations for introducing or upgrading control measures (*e.g.*, tertiary treatment, source reduction). This RA was deemed semi-quantitative as other influencing factors such as influence of climate change, hydrological data, pollutant usage or occurrence dose to be considered in a future point for estimating and predicting risk.

A general model and steps for conducting a risk assessment study is presented in Fig. 1. Correlating for the needs of the shellfish industry, the first step is the identification of hazards, where physicochemical contaminants, biotoxins, processing fails, inadequate handling and short depuration process are frequently observed (Fazil, 2005). Post identification, the contaminants and processing failures are measured and analysed to verify the severity of the potential risk; for example, if the contaminants are PTE that occur at high concentrations in shellfish waters, then represents an increased potential risk of exposure, that may also impact upon subsequent consumer safety. Next, the hazard characterization provides a better understanding of the problem and supports the development of mitigation alternatives. The fourth step in the proposed RA model reflects the development of an action plan and the main implementation of targeted measures. In the shellfish industry, the depuration process is one of the major mitigation strategies, and is mainly applied to reduce the shellfish bacterial and viral loads. Finally, the last step reflects the need for continuous monitoring of hazards identified and review of appropriate response(s); for example, Tahar et al. (2018) and Tiedeken et al. (2017) reported on the challenges limited data and lack of sufficiently sensitive analytical detection methods to inform robust RA modelling. Physical assets, such as depuration facilities, may also require upgrading to enable installation of more effective disinfection technologies for complex viral threats such as human norovirus. There is also potential to use the online graphic information system, ArcGIS, to inform the occurrence and geomapping for these targeted contaminants of concern (Tahar et al., 2018) that will inform location of concern with a view to upgrading mitigation infrastructure and assets.

In Europe, RA can be performed by permanent bodies or decentralised EU agencies and scientific communities (necessarily set up by the European Commission). A guidance to authorities is provided in the Article 20 of Regulation (EC) No 765/2008, and an implement to the risk assessment methodology described in 2015-IMP-MSG-15 (European Commission, 2016). In the United States of America, the Environmental Protection Agency (EPA) and National Research Council (NRC) provides the main guidance for risk assessment studies, separately according to the hazard and activity. International bodies such as the World Health Organization (WHO) and Food and Agriculture Organization (FAO) are also major references for risk assessment studies (Fazil, 2005; World Health Organization, 2020b). The International Organization for Standardization (ISO) is an important non-governmental organization responsible for standards, where the ISO 31000 is the international certification for risk management (ISO, 2018). In Ireland, with reference to the European and ISO guidelines, the Health Safety Authority (HSA) provides the guidance to protect employees and identify hazards (HSA, 2022).

A risk assessment is not only interesting to evaluate an ongoing activity, but essential to evaluate the environmental impact of new activities. In a recent report, the Irish Marine Institute (2020) provided a full analysis of a conservation area and its potential use for aquaculture and fishing projects. The description of *in site* activities, risks, effects and assessment through a score system were considered to endorse or reject the setting and usage of the natural habitat. The RA can be also focused on one contaminant/activity, or effect in shellfish/humans.

7. Estimated daily intake and targeted hazard quotient of contaminants in shellfish

The health risk due to contaminants in shellfish can be estimated by calculating the estimated daily intake (EDI) and targeted hazard quotient (THQ) (USEPA, 2000). First, EDI is calculated considering the concentration of contaminant in the shellfish (Eq. 1), usually expressed in $\mu g\ g^{-1}$; the daily

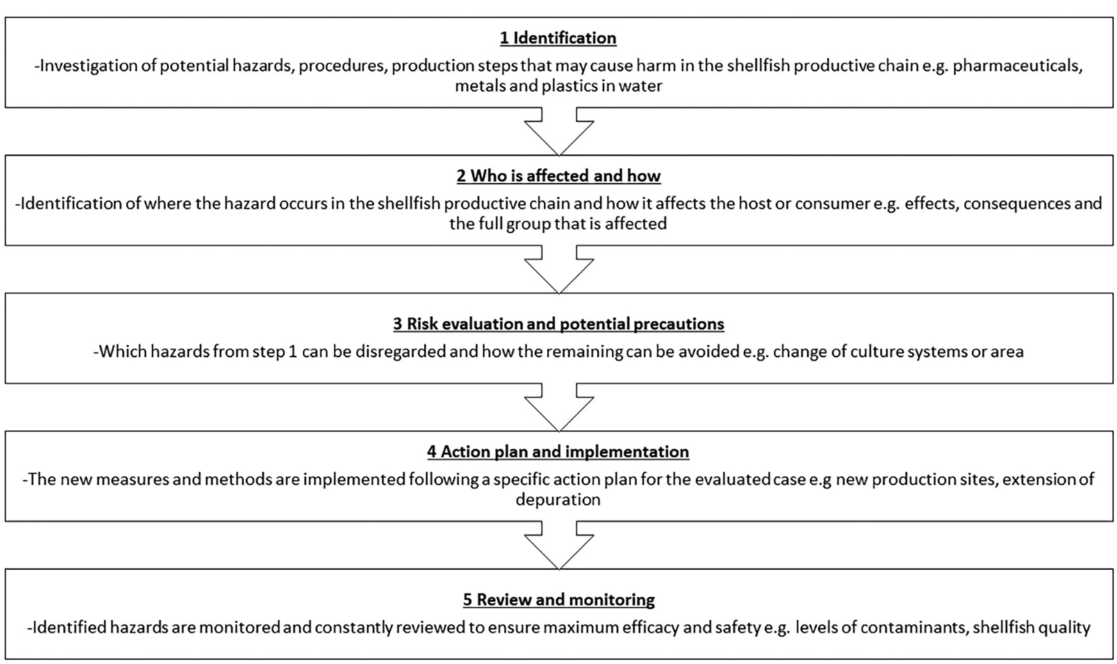

Fig. 1. General steps of a risk assessment study.

mean ingestion (DMN) expresses the daily consumption of >shellfish *per capita* in the region/area where the shellfish is mainly consumed; and the average body weight of consumer (BW).

Then, THQ (Eq. 2) is obtained considering the oral reference dose (RFd) of the contaminant, an estimate of daily exposure to low risk of deleterious effects during a lifetime (USEDA, 1991)

For estimated daily intake (EDI), concentration of contaminant in shellfish is multiplied by the daily mean ingestion and divided by average body weight:

$$EDI = \frac{C.Contaminant \times daily\ mean\ ingestion}{Body\ weight} \tag{1}$$

For targeted hazard quotient (THQ), estimated daily intake is divided by oral reference dose, resulting in a constant value for THQ:

$$THQ = \frac{EDI}{RFd} \tag{2}$$

Concentration of PHAR, PTE and MP in shellfish (Tables 1, 2 and 3) were used to simulate the EDI for adults in Europe, Africa, Asia, America and Oceania based on average population weight and shellfish consumption *per capita* (Appendix A) (Rodriguez-Martinez et al., 2020). EDI and THQ were estimated based on two scenarios: continent-specific consumption, *per capita*, of crustaceans and molluscs reported by FAO (2020), where Europe, Africa, Asia, America and Oceania consume mean values of 10.16 ± 0.23, 0.55 ± 0.2, 16.24 ± 1.77, 1.56 ± 2 and 14.24 ± 1.8 g day^{-1}, respectively; and according to USDA and USDHHS (2020) in a guide for fish and shellfish consumption that classifies species that can be consumed in 2–3 servings (maximum 340 g) a week based on low mercury levels, and 1 serving (maximum 28 g) for species with higher levels. The consumption advice released by USDA and USDHHS (2020) intends to stimulate the healthy consumption of non-contaminated seafood due to benefits as part of a balanced eating pattern. An ingestion of 3 servings of 4 oz. (340 g) of shellfish (non-pregnant adults) was chosen in a hypothetical scenario to estimate the exposure to PHAR, PTE and MP in shellfish (Tables 1–3) when consuming the recommended amount, *per capita*, of shellfish. Therefore, 48.5 g was used as reference for daily consumption. The oral RFd for metals were based on USEPA (1991, 2000), a database platform part of the Integrated Risk Information System (IRIS) to provide the risk information and assessment of chemicals. For PHAR without a RFd, the parameter (Eq. 2) was replaced by the acceptable daily intake (ADI), corresponding to the lowest daily therapeutic dose without harmful effect. Currently, RFd availability is limited to PHAR applied on agriculture and/or animals. The daily intake of MP was estimated considering the number of units and particles/g and due to absence of reference values for MP to calculate the THQ.

EDI was calculated based on PHAR, PTE and MP concentrations reported in the literature. Then, THQ of PHAR and PTE were calculated and categorized according to levels and risk: no hazard (THQ ≤ 0.1), low hazard (THQ 0.1–1), moderate (THQ 1–10) and high hazard (THQ > 10) (Lemly, 1996). The total analysis for a specific contaminant, for example EDI and THQ of Cd in male and female according to FAO and USDA daily intakes, was considered the total (100 %), and each hazard level summed to calculate the specific percentage of the total. In Figs. 2 and 3 is presented the percentage of each hazard level per contaminant. The complete dataset is available in Appendix A.

EDI and THQ (Fig. 2) were higher for simulations with USDA and USDHHS (2020) consumption profile than FAO due to recommended ingestion of shellfish being higher than current mean. The lowest daily consumption of shellfish was identified in Africa (0.55 g day^{-1}) and highest in Asia (16.24 g day^{-1}).

THQ for potentially toxic elements (PTE) is presented in Fig. 2. Highest THQ were observed in Asia, and to Cu based on the PTE concentrations reported in shellfish. THQ was lower for As and Cr, with a moderate/low risk/no hazard levels. EDI and THQ were expressively higher in studies where shellfish were sampled from severely contaminated areas as reported by He et al. (2016). The authors calculated the HQ for Cu, Cd, and Zn in *Crassostrea angulata* and *Crassostrea hongkongensis*, based on the reference doses (RfD) and estimated daily intake (EDI) as established by the USEPA (2005), considering the average body weight of a person from China and specific metal bioaccessibility (<100 %). THQ reported agreed with the

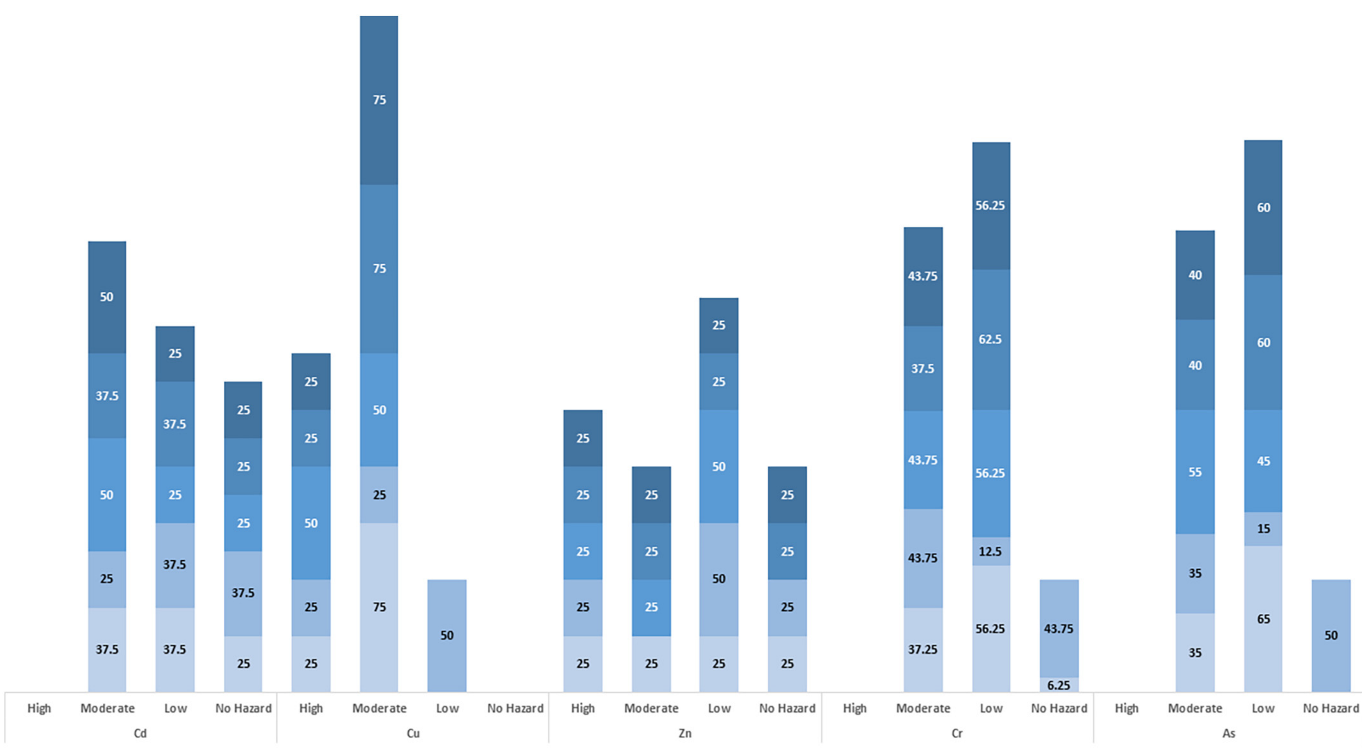

Fig. 2. Distribution of potentially toxic elements hazards (%) by continent.

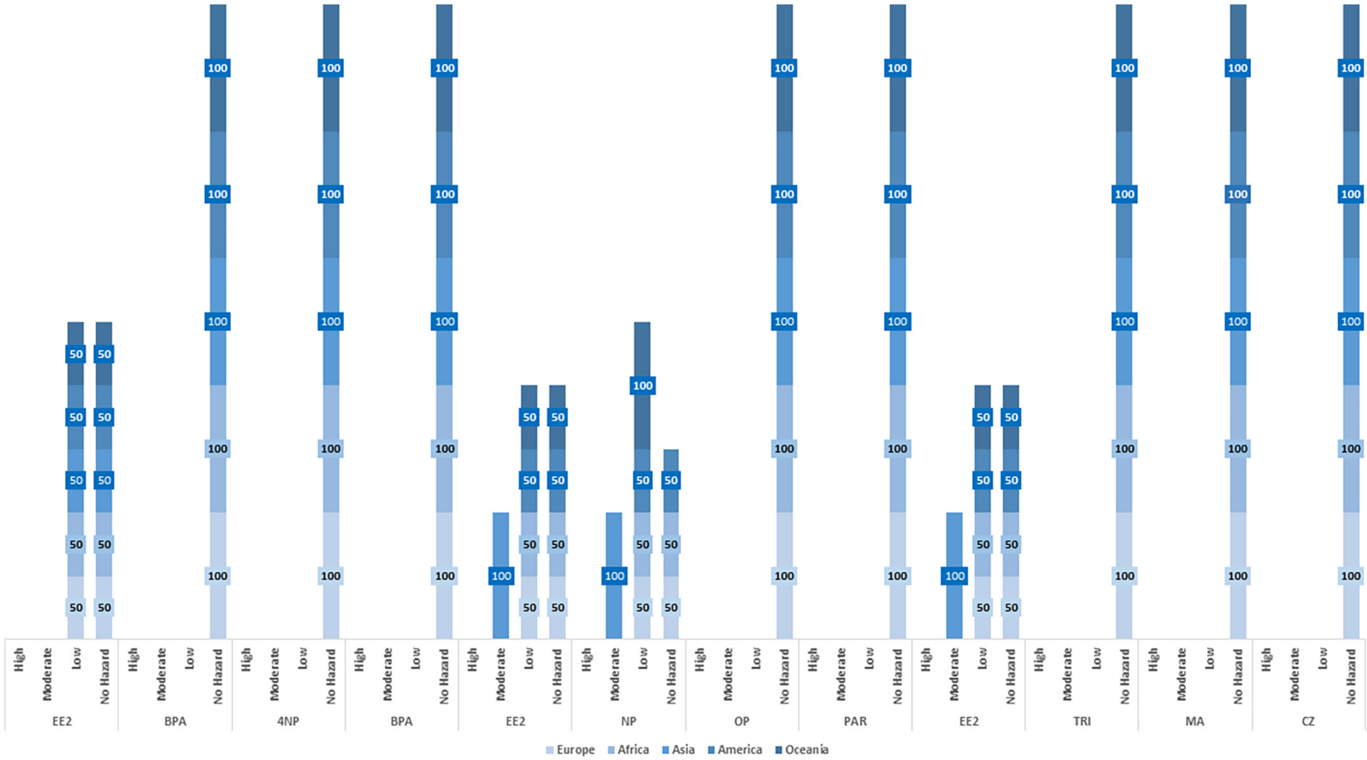

Fig. 3. Distribution of pharmaceuticals hazards (%) by continent.

authors, signalling a high/moderate risk for Cu, Cd and Zn from consuming *C. angulate* and *C. hongkongensis* with contamination levels from reported waters. Cu concentration reported by the authors led to the highest THQ (Fig. 2), with Asia having 50 % of population in a potential scenario of high exposure. Yuan et al. (2020) considered the average weight of a person from China in their study and determined the HQ, bioconcentration factor (BF), cumulative risk (AR) and carcinogenic risk (CR) of Cu, Pb, Zn, Cd, Cr, Hg, and As in *P. viridis*, *M. edulis*, *O. glomerate*, *B. virescens*, *G. divaricatum*, and *C. scripta*. The authors identified high BF for Cu and Zn, calculated by dividing the concentration of PTE in bivalves by concentration of PTE in the sampled seawater.

Yuan et al. (2020) In another study in Bosnia and Herzegovina, Djedjibegovic et al. (2020) determined the health risk of exposure to Cd, Hg, and Pb in commercial seafood products by estimating the weekly intake, hazard index, target hazard quotients, and percentage of tolerable weekly intake by adults of average weight of 70 kg over a lifetime of 70 years. No risk was identified for shellfish based on the consumption profile of adults in Bosnia and Herzegovina. El-Shenawy et al. (2016) estimated the exposure to Al, Cd, Cr, Cu, Co, Fe, Mn, Mo, Ni, Pb, Sr, V, and Zn for local consumers of *Ruditapes decussatus* and *Paphia undulata* shellfish in Ismailia, Egypt, considering the consumption rate of a specific body weight group. Fe, Al, Zn, and Sr had the highest concentration in the bivalves, and Pb was nearly two times higher than the maximum limit; however, the HQ was lower than the limit for all metals.

THQ of PHARs values are presented in Fig. 3. Highest continental exposure was identified in Asia and a similar exposure between Europe, Africa, America and Oceania. Nonylphenol (NP) was the highest hazard PHAR, with moderate to no hazard THQs. NP is a synthetic organic compound widely used in the production of surfactants with extensively estrogenic activity reported. Its persistence and high accumulation in sediments was reported by Zhang et al. (2011) with a concentration of 1964.8 ng g^{-1} in Yundang Lagoon of Xiamen, China. Asia would be more affected to pharmaceuticals in shellfish with a moderate exposure to ubiquitous contaminants such as EE2 and NP, although Europe, Africa, America and Oceania had a THQ < 1. BPA, OP, PAR, TRI, MA and CZ were not present in hazard levels (THQ ≤ 0.1) and no high hazard (THQ > 10) was observed for listed PHAs. Interestingly, concentration of BPA in different shellfish species and locations reported by Chiu et al. (2018) and Zhang et al. (2011) resulted in the same exposure level in all continents. A similar THQ for EE2 was observed by Chiu et al. (2018), Zhang et al. (2011) and McEneff et al. (2014) at different locations and shellfish species. A variety of PHARs are usually present at same time in water and shellfish. If combined and calculated as hazard index, PHARs can potentially threat consumer safety and increase its hazard level.

Mello et al. (2022) reported the occurrence of PHAR in highly consumed bivalves and at Parnaiba River Delta (Brazil) and Sepetiba Bay (Brazil). Risk assessment and human exposure were also assessed. The presence of furosemide (FUR), carbamazepine (CBZ), ketoprofen (KET), bezafibrate (BZF), ibuprofen (IBU), gemfibrozil (GFB), diclofenac (DIC), simvastatin (SIM) was identified in the bivalve species *A. brasiliana* and *M. edulis*, with a consumer daily exposure to SIM, FUR and IBU up to 10 ng kg^{-1} body weight of bivalve. *A. brasiliana* had the highest human exposure of 20.3 ng kg^{-1} body weight when considering all PHARs analysed. The estimated exposure was considered safe as target hazard quotient and hazard index were below 1 for all species and PHARs. However, only one metabolite was analysed in the study and the exposure could be underestimated. After ingestion, a drug can be metabolised by hydrolysis, oxidation, reduction and several reactions before reaching the shellfish. The constant monitoring of coastal areas and surroundings of shellfish farms is necessary to evaluate the level of contamination and register possible alterations from constant exposure to low concentrations.

The highest estimated daily exposure (EDI) to microplastics (MP) in shellfish was observed in Asia. Devriese et al. (2015) reported the presence of 0.68 microplastics/gram of shrimp. The consumption of 48.6 g of shellfish would result in the ingestion of 0.53 g of microplastics a day — approximately 1 % of shrimp weight corresponding to microplastics. Levels of microplastics in the papers analysed were not distinct by species, van Cauwenberghe and Janssen (2014) and Devriese et al. (2015) reported 0.2 and 0.36 microplastics/g of *M. edulis*, respectively. As observed in Appendix A, EDI ranged from 0.005 to 0.53 microplastics/g, an annual maximum ingestion of 193 microplastics/g of shellfish. A RA of microplastics in bivalve molluscs was recently published by Ding et al.

(2022). The authors analysed the quantitative and qualitative data from 52 peer-reviewed papers and estimated the chemical composition risk, annual dietary intake and load index of microplastics by consumption of bivalve molluscs. Polyethylene terephthalate was the most abundant polymer in bivalves (20.4 % ± 21.2 %) followed by polyethylene (13 % ± 19.2 %), rayon (9 % ± 15.6 %), polypropylene (8.9 % ± 13.3 %), cellophane (8 % ± 17.7 %), polyester (7 % ± 12.4 %) and polyamide (5.3 % ± 14.8 %). The global abundance was in the range of 0.04–20 microplastics/g. Iran, Greece and China were the three countries with the highest levels. Median intake of microplastics *via* mollusc consumption was 751 microplastics per person. Differences in mollusc consumption, microplastics abundance, culture and geography were aspects associated with the wide intake range of 15–7333 microplastics/person.

The estimation of EDI and TDH for contaminants in shellfish based on levels available in publications, reports and papers allowed the construction of two consumption scenarios: first with the recommended portion of shellfish (USEPA), and the current mean in each continent (FAO). However, there is a significant variability in the shellfish consumption between countries of the same group (continent) and it would be necessary to calculate separately to provide accurately the status of each region. The objective of calculating EDI and THD showed step-by-step how risks can be easily estimated, allowing the small shellfish producers to estimate the local exposure and support decision-making. Many contaminants can be accumulated by shellfish when farmed in contaminated areas, a higher risk when compared to single analysis. The constant monitoring of water, soil and shellfish is essential to provide accurate assessment of shellfish risk and quality and must be associated to bioavailability studies to inform the %contaminant directly available. Most of the RA conducted for the shellfish industry are related to PTE (Hantoro et al., 2019). There remains a wide diversity of contaminants (*e.g.* plastics and pharmaceuticals) that must be comprehensively studied in order to ensure development of appropriate RA to inform management and where applicable, changes to policies.

8. Conclusions

- In the present study, the environmental contaminants microplastic, pharmaceuticals and potentially toxic elements that threaten the shellfish industry were widely discussed.
- The effects and consequences in the most consumed shellfish species were highlighted and promising mitigation alternatives registered.
- Regulation and international guidelines were provided that can potentially assist decision making and contamination control.
- A panorama of Irish waters was provided. As noted in other countries, there is a gap in understanding the presence, extension of contamination and effects of the contaminants discussed.
- There is a need for the development of techniques for monitoring, standardization of risk assessments and detection of emerging contaminants in the environment.
- The reduction of contamination level in shellfish waters and employment of a risk assessment (RA) approach is essential to ensure consumer safety.
- International consensus must be reached on oral reference dose and exposure limits. There is a pressing need to simultaneously evaluate, model and predict the plethora of influencing factors governing the efficacy of RA models to inform decision making in real time.

CRediT authorship contribution statement

Gustavo Waltzer Fehrenbach: Conceptualization, Methodology, Investigation, Writing – original draft, Visualization. **Robert Pogue:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration. **Frank Carter:** Methodology, Writing – review & editing. **Eoghan Clifford:** Conceptualization, Writing – review & editing, Supervision, Project administration. **Neil Rowan:** Conceptualization, Writing – review & editing, Supervision, Project administration.

Declaration of competing interest

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Appendix A. Supplementary data

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