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Microplastic exposure, oxidative stress, and potential heme protein vulnerability in teleost fish: implications for oxygen transport and seafood quality

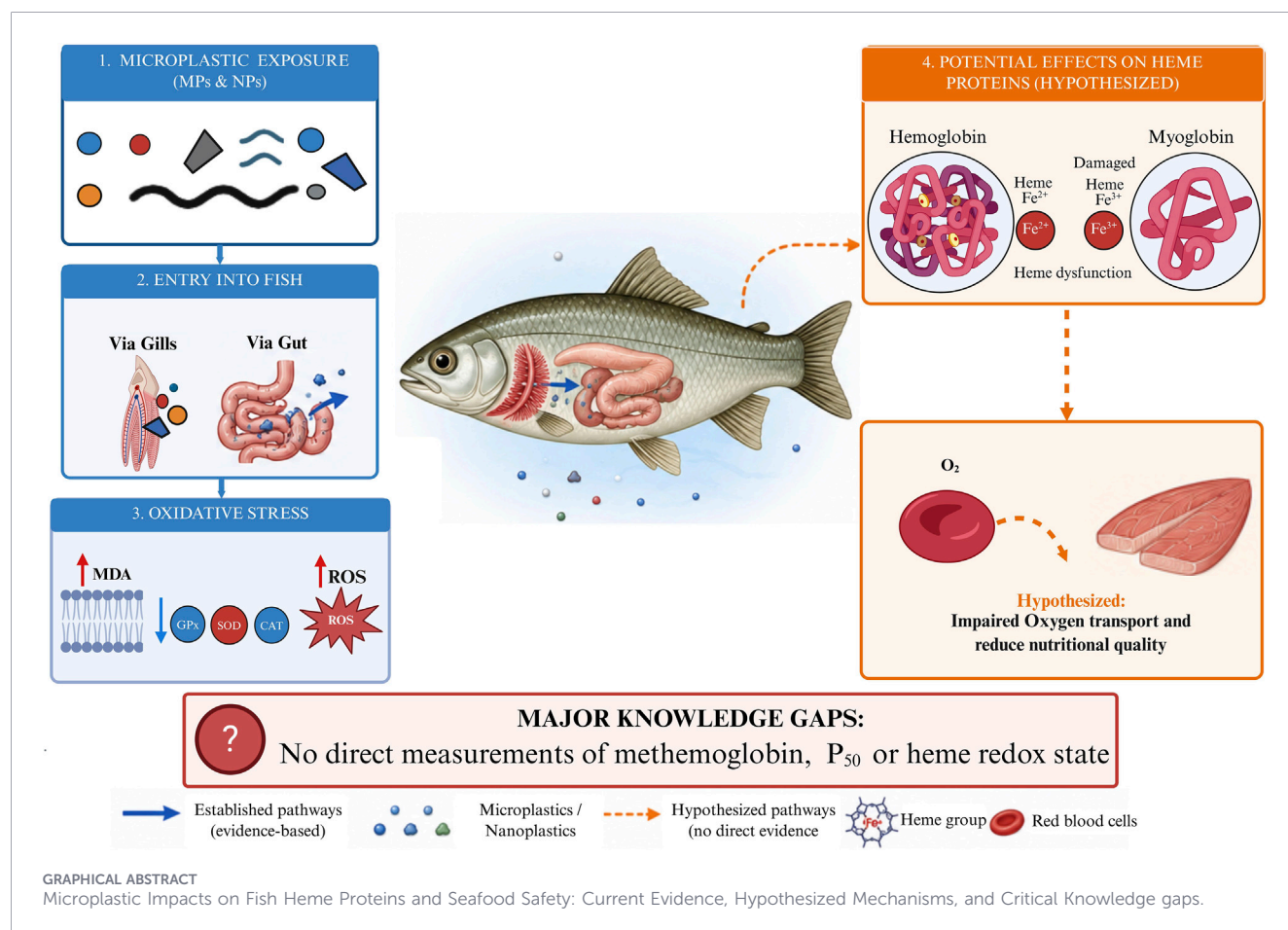
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Microplastics (MPs) are a growing concern due to the impact they have on fish physiology and safety of seafood. This review brings together recent research related MP induced oxidative stress in teleost fish and implications for muscle nutritional quality and the role of heme containing oxygen transport proteins. MPs are found primarily in the liver (32% of samples), as well as muscle, and enter fish primarily via gill uptake and ingestion. Laboratory tests consistently show increased oxidative stress markers such as malondialdehyde (MDA 1.8–3.78-fold) and protein carbonyls (1.8–2.4-fold) as well as decreased antioxidant enzyme activities (SOD, CAT, GPx decreased by 38%–52%). This oxidative imbalance could enhance the possibility of the heme iron to undergo autoxidation and globin modification, but there is no direct evidence at this time as measurements of heme iron redox state, P₅₀ values and methemoglobin generation have not been performed. Metabolomic analysis also shows changes in the levels of amino acids, such as a decrease in tryptophan and tyrosine, suggesting impaired metabolic processes with unfamiliar relevance to heme biosynthesis. This review differentiates between established oxidative and inflammatory effects and the hypothesized effects on heme proteins, and emphasizes the critical need for direct biophysical measurements such as methemoglobin, P₅₀, heme speciation to gain a better understanding of fish welfare and seafood nutritional quality.

KEYWORDS

aquatic ecotoxicology, human health risk, microplastics, nano remediation, oxidative stress, trophic transfer



1 Introduction

The production of plastics has grown exponentially worldwide, causing a widespread pollution hazard in water bodies, as it is estimated that 4.8–12.7 million metric tons of plastic waste enter the aquatic environments every year (Alberghini et al., 2022; Kershaw and Rochman, 2015). Macroplastics get fragmented into microplastics (<5 mm) through photo-oxidative and mechanical processes, and end up in all aquatic compartments, leading to microplastics as ubiquitous contaminants that spread throughout complex seafood chains (Hartmann et al., 2017; Thakur et al., 2022).

Abbreviations: ADP, Adenosine Diphosphate; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ATP, Adenosine Triphosphate; CAT, Catalase; ER, Endoplasmic Reticulum; FABP1, Fatty Acid Binding Protein 1; GPx, Glutathione Peroxidase; GRP78, Glucose-Regulated Protein 78; Hb, Hemoglobin; LDH, Lactate Dehydrogenase; Mb, Myoglobin; MDA, Malondialdehyde; MP, Microplastic; NP, Nanoplastic; PC, Protein Carbonyl; PCV, Packed Cell Volume; PERK, Protein Kinase R-like Endoplasmic Reticulum Kinase; PPARγ, Peroxisome Proliferator-Activated Receptor Gamma; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RBC, Red Blood Cell; ROS, Reactive Oxygen Species; SCD1, Stearoyl-CoA Desaturase 1; SOD, Superoxide Dismutase; TAC, Total Antioxidant Capacity; UPR, Unfolded Protein Response.

Particles have the potential to be significant bioindicators of aquatic pollution and major vectors of anthropogenic dietary exposure because teleost fish are constantly exposed to the water and are opportunistic feeders (Mercogliano et al., 2020; Su et al., 2019). In addition to providing ecological warning signs, fish are a major source of animal protein for the world, providing around 20.5 kg *per capita* per year, a protein essential for the livelihoods of billions of people across the globe (Action, 2020; Golden et al., 2016). Preservation of structural and functional proteins plays a key role in determining the nutritional integrity and commercial qualities of fishery products, as these proteins are crucial for muscle development, metabolic homeostasis and post-harvest qualities (Subaramaniyam et al., 2023; Thilsted et al., 2016). This narrative review synthesizes the peer-reviewed literature concerning the toxicity of microplastics to fish. Literature was searched by using specific search terms in the major databases that were developed to search for studies reporting on oxidative stress, metabolic disruption, histological changes, and bioaccumulation in teleost fish. A formal PRISMA protocol was not used because the aim of this research is not to carry out a systematic meta-analysis, but a hypothesis-oriented critical review. Some of the key constraints addresses, are the lack of direct biophysical measurements, species variability, the lack of ecological relevance of tested

exposure concentrations, and the difference between micro and nanoplastics in the results. Multiple toxicological cascades have been consistently observed in both laboratory and field studies after ingestion of microplastics, such as dose-dependent lipid peroxidation and proteotoxicity. Polypropylene and polystyrene microplastics increase malondialdehyde, protein ubiquitination, and decrease the level of amino acid precursor (Lee et al., 2023; Lusher et al., 2020). Although oxidative stress has been well documented, mechanistic study of the susceptibility of respiratory heme proteins is missing. This review assesses the possible mechanisms of microplastic-induced oxidative stress and its impact on the susceptibility of heme proteins, reduced capacity to transport oxygen, and altered nutritional value of seafood.

This review is unique because it focuses on the heme part of hemoglobin and myoglobin, and suggests that microplastics may create oxidative stress on these molecules. It clearly distinguishes between the well-established oxidative and inflammatory responses and the postulated changes in heme protein structure, redox state, oxygen binding and nutritional bioavailability. This review also critically examines the pros and cons of the existing knowledge regarding the toxicity of micro-plastics in teleost fish, especially focusing on the oxidative stress response. Clearly distinguishes facts from effects on heme proteins. This synthesis points to some gaps in the literature, including methodological difficulties like high doses of laboratory research, pure particles, and the absence of direct measurements of heme-related parameters, and presents an organized basis for future studies.

1.1 Literature search and review methodology

This manuscript is a narrative critical review of the evidence available about the effects of microplastic exposure on teleost fish, with a specific focus on oxidative stress responses and potential implications for heme protein function. A formal PRISMA protocol was not applied as it is not possible for a narrative review. Literature was systematically searched in major databases such as PubMed, Web of Science, Scopus, and Google Scholar from 2015–2026. The primary search used the following combined search terms: “microplastic” OR “nanoplastic” OR “microplastics” OR “polystyrene” OR “polypropylene”) AND (“fish” OR “teleost” OR “Sparus” OR “Dicentrarchus” OR “Carassius” OR “Oreochromis”) AND (“oxidative stress” OR “antioxidant” OR “MDA” OR “SOD” OR “CAT” OR “heme” OR “hemoglobin” OR “myoglobin” OR “oxygen transport” OR “bioaccumulation” OR “toxicity”). Further searches were performed that included the terms “microplastics heme”, “microplastics methemoglobin” and “microplastics nutritional quality fish”. Based on inclusion/exclusion criteria described above, studies have been selected and the ones with exposure details and quantitative oxidative stress biomarkers have been given priority. Positive and negative findings were taken into consideration in the synthesis process, but since this is a narrative review, there was an emphasis on studying consistent patterns to generate mechanistic hypotheses. Limits are indicated in Section 3.5 for the case of no significant effects or weaker responses at lower concentrations as reported by studies. The microplastic dose range of laboratory studies reviewed was 10 µg/L to 800 µg/L and the nanoplastics dose range was 0.2 mg/L to 4 mg/L; and most of the

studies were of acute or sub-chronic duration (7–30 days). The concentrations found in the field (see Figure 1B; Section 3.5) are typically orders of magnitude smaller. This narrative approach does not prevent any possible selection bias, but was selected to offer a hypothesis-driven critical examination instead of a quantitative meta-analysis.

Where there was a quantitative outcome, it is displayed in the terms that were reported in the original paper (fold-change, percentage change or upregulation/downregulation). Fold changes are also highlighted when available to emphasize that the effect size is a standardised measure of effect, giving readers the appreciation for consistency and strength of oxidative stress responses regardless of the variability in exposure conditions. If percentages or qualitative terms were only provided, they are included as reported. This hybrid method is based on the heterogeneity of the primary literature, but highlights the common trends such as higher MDA, lower antioxidant enzyme activities. Values are reported in tables and figures with the original context (species, polymer type, concentration and duration) included to facilitate interpretation of the data.

2 Heme proteins in fish: structure, function, and nutritional relevance

2.1 Structural organization of hemoglobin and myoglobin

The hemoglobin and myoglobin of fish are two structurally specialised oxygen binding proteins that play a key role in respiratory efficiency and in post-harvest tissue quality. The teleost hemoglobin is composed of $\alpha_2\beta_2$ globin chains that coordinate the Fe²⁺-heme within hydrophobic pockets, where myoglobin is a monomeric oxygen storage protein that has a higher affinity (Storz, 2018; Trefts et al., 2017). Although these proteins are important for function, no study directly characterizes structural changes in these proteins after exposure to microplastics. The current evidence is only indirect oxidative markers including protein carbonyls following exposure to polypropylene, and ER stress following exposure to polystyrene (Acarer Arat, 2025; Del Piano et al., 2024). The results suggest a pro-oxidant environment which could impact on heme proteins, but a direct spectroscopic confirmation of the oxidation of Fe²⁺ or destabilization of the heme pocket is not yet available. Advanced biophysical tools are needed to resolve heme-specific vulnerability in an ecotoxicological context.

2.2 Physiological roles in fish metabolism

There are two different but complementary functions for hemoglobin and myoglobin in fish oxygen metabolism. The erythrocyte contains a tetrameric protein called hemoglobin that mostly transports oxygen from the gills to tissues, where the muscle cell contains a monomeric protein (myoglobin) that transports and stores oxygen inside the cell (Fago, 2017; Trefts et al., 2017). Available indirect evidence indicates that exposure to microplastics may cause conditions that compromise the efficiency of oxygen transport. For example, the combined exposure of nitrite (20 mg/L) and polystyrene microplastics

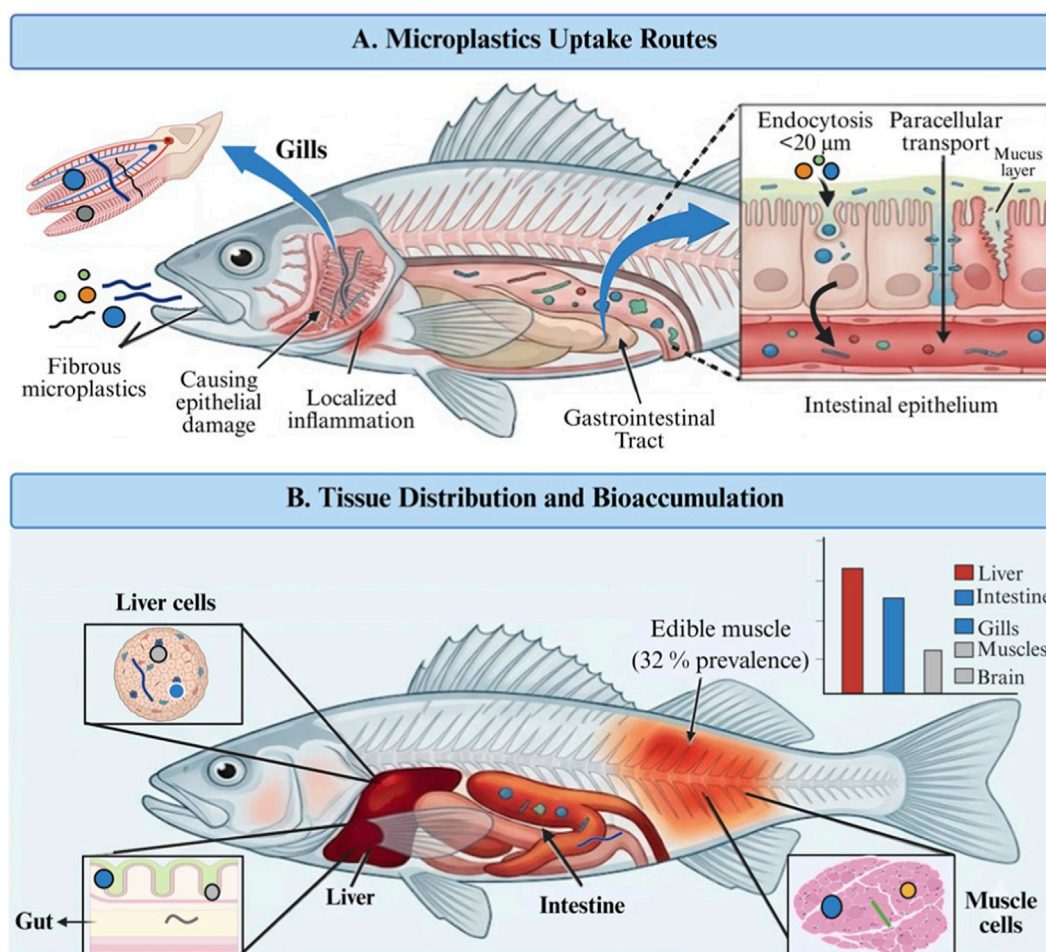


FIGURE 1
Pathways of microplastic uptake, tissue distribution, and bioaccumulation in teleost fish, highlighting translocation to edible muscle tissue. (A) Microplastic uptake routes. (B) Tissue distribution and bioaccumulation.

(10 $\mu\text{g/L}$) caused a reduction in antioxidant enzyme activities (SOD, CAT, GPx decreased 38%–52%) and led to metabolomic changes, such as decrease in amino acids (tryptophan $-1.66 \log_2$; tyrosine $-1.35 \log_2$) (Xing et al., 2023). These reductions do not represent direct steps down the classical heme biosynthesis pathway that starts with glycine and succinyl-CoA, but rather may represent effects of the oxidative stress and general metabolism. Heme iron autoxidation is also promoted by polystyrene nanoplastics (0.2–4 mg/L), which also caused an increase in malondialdehyde and protein carbonyls, thus adding to the pro-oxidant environment (Das et al., 2025). But no research has directly quantified the hemoglobin oxidation endpoints, like the amount of methemoglobin in fish exposed to microplastics, the amount of Fe^{2+} oxidized to Fe^{3+} , oxygen-binding affinity (P50), or the Bohr effect. In other biological systems ROS has been shown to promote hemoglobin autoxidation, but this mechanism has not been tested in the case of microplastic exposure in teleosts. The changes in metabolomics such as PPAR γ was upregulated by 2.1-fold, whereas FABP1 and SCD1 were downregulated by 0.4-fold and 0.6-fold, respectively further suggest altered mitochondrial and lipid metabolism, but no direct links to heme biosynthesis or hemoprotein function are provided (Kögel et al., 2020; Prüst

et al., 2020; Xing et al., 2023). Overall, oxidative stress is a uniform finding, but there is a need to assess potential heme affinity or myoglobin storage defects by integrated respirometry and real-time heme spectroscopy (Rashid et al., 2025).

2.3 Nutritional significance

Fish is a source of high-quality protein as well as highly bioavailable heme iron which is crucial for human erythropoiesis and neurodevelopment (Alberghini et al., 2022; Subaramaniyam et al., 2023). Generally, heme iron is more readily absorbed than non-heme iron (Moustarah and Daley, 2024). But there are no direct studies that quantify the loss of heme iron content, digestibility or bioavailability in microplastic-intoxicated fish. In some exposures, indirect evidence of potential impairment like protein carbonylation and increased ubiquitination suggests that the potential for oxidative modification of hemoproteins in muscle could lead to decreased heme iron release during digestion. The effects of these in sea food containing micro-plastics has never been tested (Kögel et al., 2020; Lusher et al., 2020). A second consequence of microplastic ingestion on human iron bioavailability is not quantified and is a key translational research gap. *In vitro* gastrointestinal digestion

models need to be used in future studies with uptake assays to assess any potential nutritional consequences.

2.4 Interspecific variability in fish responses to microplastics

There are considerable physiological differences in teleost fish that can affect their response to microplastic stress. There are significant differences in antioxidant capacity, hemoglobin isoforms and polymorphism, hypoxia tolerance, metabolic rate, and osmoregulatory strategies, such as the Root effect that occurs in many teleosts and results in the hemoglobin being able to bind oxygen even at low pH. Hypoxia-tolerant species, for example, *Carassius auratus* (crucian carp) might have stronger antioxidant defense than more hypoxia-sensitive species, such as *Sparus aurata* (gilthead seabream) or *Dicentrarchus labrax* (European seabass). Similarly, gill morphology, feeding habits and intestinal barrier integrity show significant inter-individual variation, influencing MP uptake and translocation efficiency. Most studies have been conducted on comparatively few model species (*C. auratus*, *Oreochromis* spp., *Danio rerio*), making the findings in these species difficult to extrapolate to other fish species. Due to these differences, responses to the same polymer type and concentration may vary from species to species (Jovanović, 2017; Lushchak, 2016; Lusher et al., 2020; Scott and Dalziel, 2021; Wootton et al., 2021). Therefore, this review highlights the common characteristics of oxidative stress, the findings should not necessarily be applied to all teleosts. Further studies should focus on multi-species comparisons and ecologically relevant models to gain insight into species-specific risks of oxygen transport physiology and muscle quality.

3 Microplastic exposure pathways and bioaccumulation in fish

3.1 Sources and types of microplastics

Microplastic (MP) proliferation is either caused by deliberate use of microplastic particles (<5 mm) or by fragmentation of larger debris; persistence and the biological interactions of the proliferation depend on the polymer type and morphology (Hartmann et al., 2017). Variability of environmental loading is significant and ranges from $259,310 \pm 57,096$ to $1,304,811 \pm 609,426$ particles/km² in the North Adriatic Sea with vertical stratification depending on density and biofouling (Viršek et al., 2017). The most dominant polymer in polymer profiles is polyethylene (PE, 66.8%–75%), followed by polypropylene (PP, 9.3%–20.7%) and polyamide (>2.6%), based on the production volumes and resilience which increase the surface residence time (Int-Veen et al., 2021; Viršek et al., 2017). But most of the laboratory studies have used pure polystyrene (PS) microspheres that do not mimic the heterogeneous, weathered field particles. In experiments, the most common shape is spheres, and in the environment the most common shapes are fibers and irregular fragments. This mismatch reduces toxicological relevance due to increased contaminant adsorption capacity, hydrophobicity, and oxidation ability of the old particles. Further changes in surface charge and uptake dynamics occur from physicochemical aging

(Van Seville et al., 2020), but have not been tested for their relation to heme protein vulnerability. This means that existing models which focus on MPs as passive particles ignore their dynamic redox-modulating properties, highlighting the need for ecologically realistic exposure systems using mixtures of polymers.

3.2 Differences between microplastics and nanoplastics

MPs (1 µm–5 mm) and NPs (<1 µm) behave and interact very differently in the environment and with organisms. Nanoplastics are more taken up into cells, translocated in the body and able to cross biological barriers such as epithelial and blood-brain barrier due to their small size and high surface area-to-volume ratio (Lee et al., 2023; Zhao et al., 2023). Larger microplastics, on the other hand, are more likely to cause mechanical damage to gills and gut at the local level. Laboratory research indicates that nanoplastics may lead to greater responses in terms of oxidative stress at lower mass concentrations than microplastics. But the majority of the research is still on microplastics, and comparisons between the various studies are still limited. This size difference has implications for the vulnerability of these heme proteins, particularly with respect to the efficiency of the nanoplastics into muscle tissue.

3.3 Uptake routes

The primary routes of uptake of microplastics in fish are through gastrointestinal ingestion and gill filtration, and are controlled by particle size, hydrodynamics, and feeding behavior. The dominant mechanism is ingestion, where the biofilm-coated MPs resemble prey cues, so improving ingestion (Ahrendt et al., 2020). Smaller MP s (<20 µm) can enter the intestine via the intestinal epithelium both by endocytosis and paracellular pathways, while larger MP s deposit in the gut, lead to villi atrophy, obstruction and poor absorption (Lei et al., 2018; Peda et al., 2016). At the same time, gills are important entry points, and fibrous MPs (~1,041 µm) are trapped at the interlamellar space, causing epithelial damage, mucous production, and inflammation (Zheng et al., 2024). Uptake efficiency and retention is determined by the particle size and not shape. However, in experimental models' exposure routes are usually isolated, and the combined respiratory, dietary dynamics, and natural flow conditions are not taken into account. Gill-associated MPs may pass in hours to days, while intestinal particles last longer, leading to dysbiosis and decreased growth. The intestinal retention leads to ER stress and barrier disruption, allowing for nanoplastic translocation, while gill inflammation results in oxidation of nearby proteins by ROS (Ma et al., 2021; Müller, 2021). There are no integrated multi-route exposure models which would allow to assess accurately the cumulative oxidative stress on heme proteins, so requiring flow-through systems that mimic natural conditions.

3.4 Tissue distribution and bioaccumulation

Once epithelial translocation occurs, microplastics spread through circulatory routes in the body, with larger particles (>20 µm) mainly localized in the liver and intestine, and the

nanoforms have a higher ability to cross the biological barrier to systemic distribution (Pitt et al., 2018). Nanoplastics are able to enter the tissues more efficiently than microplastics, and can enter neural and muscular compartments, a far broader tissue type. MPs are detected in edible muscle tissue, mostly in the form of particles. Field surveys report far lower, environmentally realistic, concentrations than many of the reported laboratory concentrations. These high doses are useful for mechanistic hazard identification but can overestimate risk and mask some subtle chronic effects that are relevant to natural settings. Furthermore, the majority of the studies are based on pristine particles and not on aged environmental MPs, which are composed of multiple polymers, and further hinder translation. Exposure studies and mixture studies need to be a research priority using environmentally realistic exposures to better inform potential effects on heme protein function and seafood quality. A summary of the main processes of microplastic interactions with fish is shown in Figure 1. The main uptake routes are shown in Panel A (Figure 1A) but with a particular focus on the ubiquitous fibre-shaped (fibrous) microplastics in the environment. Panel B (Figure 1B) illustrates the distribution and bioaccumulation of microplastics in tissues; these are commonly found in the liver but at lower levels in muscle. This visualization also highlights the differences between high laboratory concentrations and field-based environmental concentrations that have been reported.

3.5 Overview of exposure concentrations, species coverage, and polymer trends

Both laboratory and limited field studies were included in this review. Most of the evidence of oxidative stress biomarkers and the mechanisms is derived from controlled experiments in the laboratory. There are fewer field studies which are very useful for contextualizing actual exposure conditions and bioaccumulation (Viršek et al., 2017; Zheng et al., 2024). Lab studies focus mostly on high dose exposures of pristine particles of polystyrene (PS) or polypropylene (PP) with acute or sub-chronic exposures. The concentrations used are often in the range of 10 µg/L to 800 µg/L (and up) for microplastics and 0.2–4 mg/L for nanoplastics, and for dietary exposures are in the range of 25–250 mg/kg bw. At these higher doses, stronger biological effects (such as an increase in MDA by 1.8–3.78 times, an increase in protein carbonyls by 1.8–2.4 times, a decrease in SOD, CAT and GPx by 38%–52%) are generally seen, while lower doses may cause weaker or non-significant responses. Surprisingly, values in the tens of thousands of particles per km², as reported in field studies, are much lower than those used here, reaching up to a few high millions of particles per km² for surface waters (259,310 ± 57,096 to 1,304,811 ± 609,426 particles per km² in the North Adriatic Sea) and consequently the corresponding particle burdens in fish tissues (Abdolahpur Monikh et al., 2023; Koelmans et al., 2022; Kögel et al., 2020; Prüst et al., 2020; Suaria et al., 2016). The studies show that the natural environment is more dominated by fibers and weathered particles, in comparison with the lab-based spherical particles.

The extrapolations from the laboratory are based on standardized conditions and give a mechanistic understanding of the effects, but unrealistic exposure durations, doses, and pristine particles may overestimate effects. Field observations better

represent the reality of chronic, low dose and multi-stressor exposure but are confounded by other factors and have reduced statistical power. Extrapolation to natural conditions and to the potential effects on heme protein function and seafood quality needs to be done with caution. Throughout this review, these constraints are recognised, especially in the section on knowledge gaps. Most of the studies have been conducted in only a few model fishes (*C. auratus*, *D. rerio*, *Oreochromis* spp., *S. aurata*, *D. labrax*) limiting the scope of the generalizability of the findings across a wider teleost diversity. Other polymer statistics show that there is a mismatch between tested (mostly PS/PP) and environmental (PE, PP, fibres, mixtures) particles. Older and weathered/sedimented particles are underrepresented in experimental designs. The patterns indicate that there is a need for additional ecologically relevant studies that incorporate realistic concentrations, chronic exposures, and mixtures of particles and more diverse species to more adequately evaluate fish physiology and seafood safety.

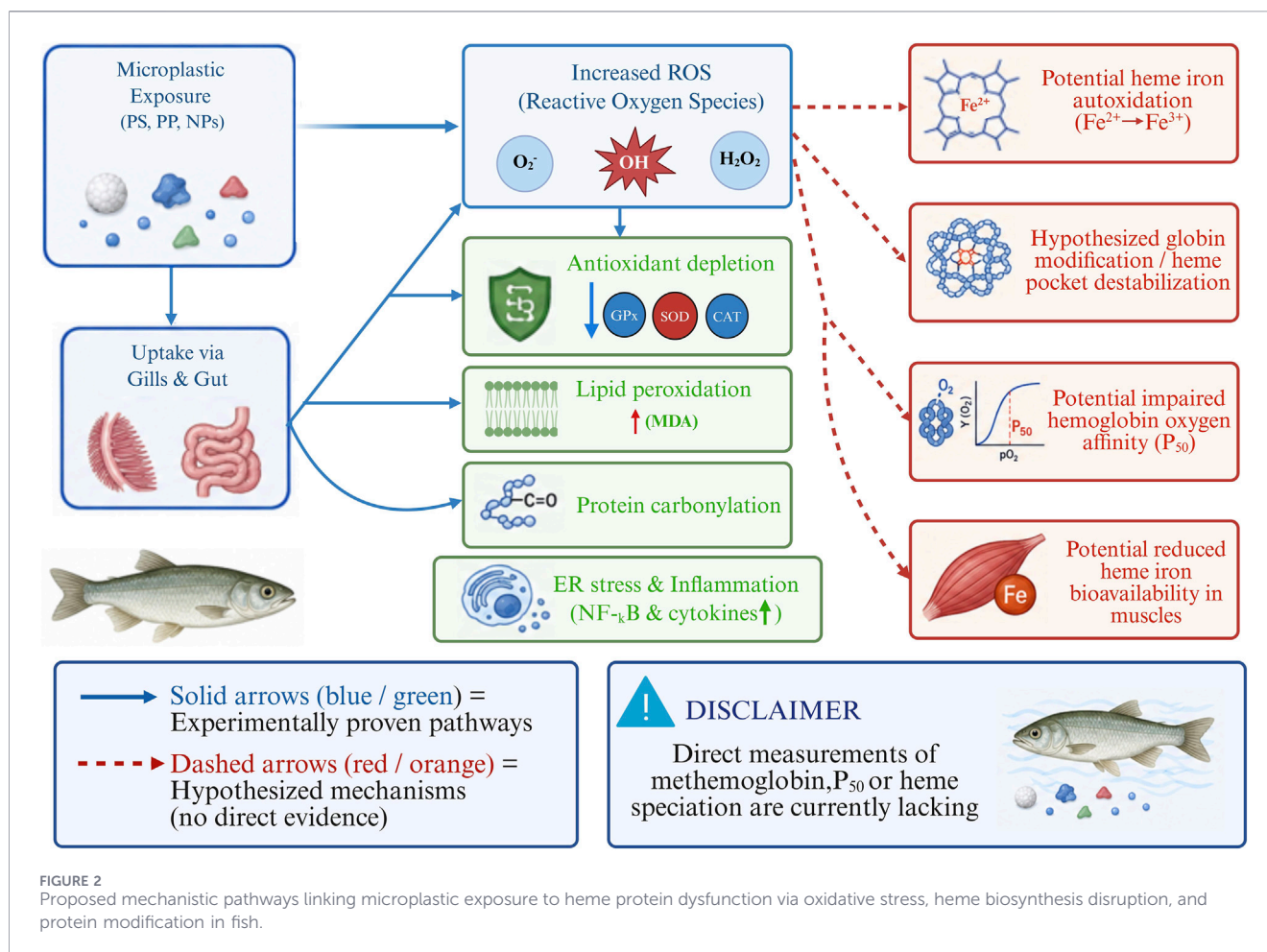
4 Mechanistic pathways linking microplastics to heme protein dysfunction

4.1 Oxidative stress and ROS-Mediated heme oxidation

The oxidative stress response to microplastic exposure is a well-established response in fish. Nano plastics in particular have a large surface area to volume ratio, which means that they can elicit stronger cellular responses than larger microplastics. Polystyrene nanoplastics (0.2–4 mg/L) exposure reduced the activity of antioxidant enzymes (SOD, CAT and GPx) by 1.66–3.78-fold and elevated malondialdehyde (MDA) and protein carbonyls (PC) by 1.66–3.78-fold (Cui et al., 2024; Das et al., 2025). These markers are generic indicators of oxidative stress and/or lipid/protein damage which are found in a variety of environmental stressors. This pro-oxidant environment could be expected to enhance the autoxidation of heme iron (Fe²⁺ to Fe³⁺) or the modification of globin, but there is no evidence that this is a cause-and-effect relationship. There are no direct measurements of heme specific outcomes such as methemoglobin levels or changes in O₂ binding affinity. The effects of larger-sized microplastics may be more localised in gills and gut, while nanoplastics may have more systemic effects through the capacity of inducing oxidative stress. Whether the oxidative stress responses are adaptive hormetic, such as upregulation of antioxidants or pathological, is still unclear. Some responses at low environmentally relevant concentrations may be compensatory while the high laboratory concentrations may overwhelm the cellular defenses (Kögel et al., 2020; Lee et al., 2023).

4.2 Interaction with adsorbed toxicants

Microplastics act as chemical vectors, co-transporting contaminants which can exacerbate the effects of oxidative stress because of their combined effects. These particles derived from fields can bind bisphenol A, polycyclic aromatic hydrocarbons and metals including Cu, Pb and Zn, that can be released in the gut (Alberghini et al., 2022; Rochman et al., 2019). Transition metals catalyze



Fenton-like reactions, which increase ROS formation. The synergism with mercury and other pollutants has been confirmed by co-exposure studies, which has shown the extent of oxidative damage (Barboza et al., 2018). Cytochrome P450 activity could be further affected by endocrine disruptors. With the aging of MPs, this effect is enhanced by greater hydrophobicity and affinity for contaminants. Though these synergistic effects have been noted, no direct characterization of heme specific modifications has been included.

4.3 Disruption of heme biosynthesis pathways

Hepatic function and endoplasmic reticulum homeostasis are disrupted by microplastic exposure, and this could impair mitochondrial heme biosynthesis. Polystyrene MPs activate PERK-eIF2 α -ATF4 pathway and inhibit mitochondrial biogenesis (Pan et al., 2021). Amino acids like tryptophan and tyrosine have been noted in metabolomic studies. Although the classical heme biosynthesis pathway starts with glycine and succinyl-CoA, these changes may be indicative of a general metabolic disruption (Zhao et al., 2020). These observations may indicate that there is one or more limiting step in the synthesis of hemoprotein, but no quantification of porphyrin intermediates has been made, which prevents the resolution of pathways for synthesis versus degradation.

The exposure to microplastics always results in oxidative stress by several pathways, as summarized in Figure 2. The intensity of these responses such as fold changes in MDA and antioxidant enzymes is representative of those observed in a number of species that are commonly studied under laboratory conditions. These reactions, however, may vary greatly in intensity and type with different species of teleosts, concentrations of exposure, particle type and length of exposure. For information about exposure parameters and species coverage, readers are encouraged to refer to Section 3.5.

4.4 Protein conformational changes and denaturation

If oxidation occurs during the process, it could be a mechanism for the destabilization of globin structure, while direct or indirect polymer-protein interactions are also a potential mechanism, as discussed in Table 1. In the case of polypropylene microplastics, they have been found to enhance ubiquitin conjugates, thereby altering autophagic flux, indicating selective removal of misfolded proteins (Missawi et al., 2022; Priyadharshini et al., 2024). The critical amino acid residues may also undergo carbonylation, which could impact on the coordination of the heme and the folding of globins. These effects can be further exacerbated by inflammatory responses with bursts of ROS production and production of cytokines. Moreover, apoptotic signaling has also been linked to increased protein

TABLE 1 Oxidative stress responses and potential links to heme protein vulnerability in fish.

Biological endpoint	Biomarker	Quantitative evidence	Mechanistic interpretation (proven)	Evidence level	Hypothesized heme protein relevance	References
Antioxidant defense	SOD, CAT, GPx activity	Decreased by 38%–52%	Antioxidant depletion leading to ROS accumulation	Proven	Increased vulnerability of heme iron to autoxidation (hypothesized)	Das et al. (2025)
Lipid peroxidation	MDA	Increased by 1.66–3.78-fold	ROS-mediated lipid damage	Proven	Pro-oxidant environment potentially favoring heme oxidation (hypothesized)	Cui et al. (2024), Das et al. (2025)
Protein oxidation	Protein carbonyls	Increased by 1.8 = 2.4-fold	ROS-mediated protein carbonylation	Proven	Possible destabilization of globin structure (hypothesized)	Bobori et al. (2022)
Metabolic disruption	Tryptophan, Tyrosine	Decreased by 1.35–1.66 log ₂ -fold	General amino acid depletion	Proven (metabolomics)	Indirect effect on heme biosynthesis unlikely (tryptophan is not a direct heme precursor)	Xing et al. (2023)
Ubiquitin proteasome system	Ubiquitin conjugates	Increased by 2–3-fold	Increased protein degradation	Proven	Potential loss of functional Hb/ Mb pools (hypothesized)	Bobori et al. (2022)

degradation rates, such as globin chain (Hirt and Body-Malapel, 2020; Lee et al., 2023). But there is only circumstantial evidence that these changes are related specifically to heme proteins. It has relied solely on general proteomic markers of proteostatic stress and has not been directly validated by structural studies such as X-ray crystallography, circular dichroism or resonance Raman spectroscopy which can confirm changes in the globin chains conformation and changes in heme coordination. There are no studies showing specific changes in the tertiary/quaternary structure of hemoglobin and/or myoglobin after exposure to microplastics in fish. These possible mechanisms need to be tested through future biophysical studies.

5 Functional consequences: oxygen transport, muscle physiology, and fish health

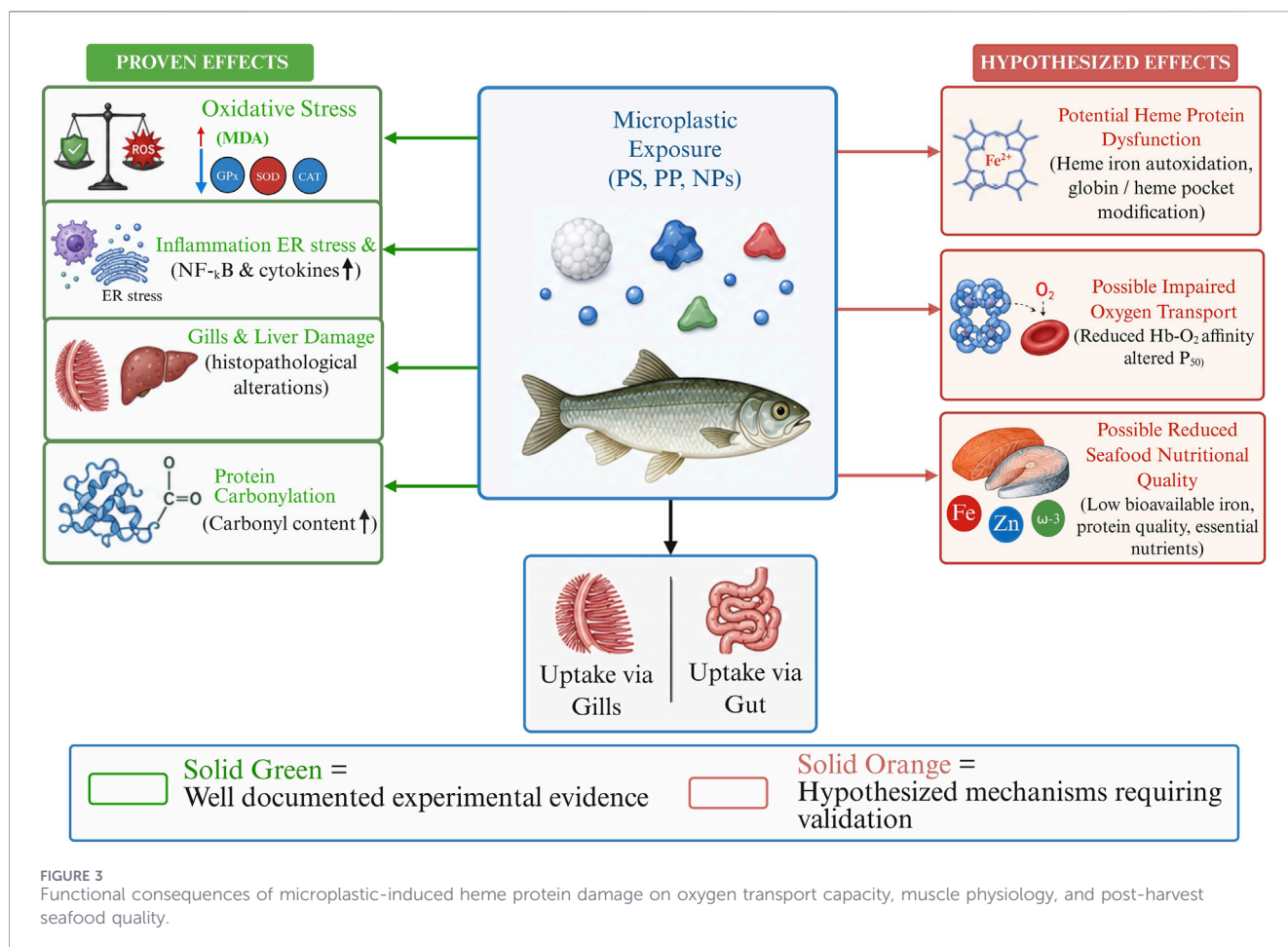
5.1 Alterations in hemoglobin concentration and hematological indices

Exposure to microplastics affects fish hematology, with inconsistent and non-standardized responses. Polystyrene nanoplastics, which cause metabolic stress, lead to a reduction in total protein, as well as in albumin, while increasing glucose and alkaline phosphatase, which may indirectly affect erythropoiesis. Similarly, exposure to both nitrite and MP cause elevated AST and ALT, indicating damage to the liver’s hepatocytes and possible disruption of circulation (Azarm-Karnagh et al., 2025; Brun et al., 2019). There are few direct measurements of red blood cells, hematocrit or hemoglobin concentration. While oxidative damage has been documented under exposure of polypropylene, comprehensive and quantitative analysis of hematological indices is not common. Secondary evidence is available to support the relationship of the decreased RBC parameters to diminished oxygen transport and anemia-like effects, but it has not been

validated for microplastics (Ghosh, 2025; Nair and Perumal, 2024). The variation in the studies might be due to the differences in the duration of exposure, size of exposure particles, types of polymers, and sensitivity of the species in each study. Microvascular function and oxygen delivery may be further decreased in inflammatory conditions, regardless of hemoglobin. Although there is evidence of oxidative and inflammatory stress, there are no studies that measure oxygen-binding parameters and thus cannot mechanistically link hematological disruption to functional hypoxia (Viršek et al., 2017; Zarantonniello et al., 2024).

5.2 Impairment of oxygen-binding capacity

The effects of microplastics on the oxygen affinity of hemoglobin and on oxygen delivery to the body are not yet fully known (Piccardo et al., 2026). Exposure to polystyrene induces ER stress, ROS generation and lipid peroxidation, which promote hemoglobin autoxidation and methemoglobin formation in other systems (Hirt and Body-Malapel, 2020). Nanoplastics are known to induce a pro-oxidant state by inhibiting antioxidant defences and increasing malondialdehyde, potentially affecting oxygen binding (Kögel et al., 2020; Lusher et al., 2020). Functional interpretation is hampered by the fact that no study has measured the oxygen-binding parameters (P₅₀) and the Bohr effect (ATP, GTP, Cl[−]) in MP exposed fish. Additionally, metabolomic depletion of nicotinic acid and tryptophan could further indicate lower redox buffering capacity in erythrocytes (Kögel et al., 2020; Lusher et al., 2020). Time of exposure matters, with acute stress being associated with oxidative bursts and prolonged stress associated with metabolic reprogramming. Hypoxia can also be worsened due to increased inflammation, which can reduce microvascular perfusion without affecting hemoglobin affinity, as shown in Figure 3. Based on the field observation of gill damage and the presence of microplastics, the compromised uptake of oxygen is supported, but not attributed to hemoglobin-specific effects (Zheng et al., 2024). In summary, mechanistic connections between heme oxidation and functional



hypoxia are not well made due to the lack of direct biophysical measurements.

5.3 Myoglobin oxidation and muscle quality deterioration

Although there is little direct evidence of myoglobin oxidation causing quality deterioration, it is clear that exposure to microplastic causes oxidative stress in the body overall, probably including in skeletal muscle (Yang et al., 2024). The NPs cause an increase in malondialdehyde and protein carbonyl levels, and decrease the activity of antioxidant enzymes, which increases the levels of oxidative stress in myoglobin (Kumar et al., 2022). The transformation of Fe²⁺-myoglobin to Fe³⁺ (metmyoglobin) can initiate brown discoloration and promote lipid peroxidation that affects the texture, water-holding capacity, and shelf-life of the final product. Microplastics may be restricted to the gut, but micro-sized species eaten whole pose a greater risk of exposure, as discussed in Table 2 (Rizaldi et al., 2025; Smith et al., 2018). The metabolomic changes signify altered protein metabolism and mitochondrial function, which could impact post-mortem metabolism and meat quality. But there is no study on the measurement of myoglobin redox status and standard quality indices (color, texture, storage stability) in MP exposed fish (Hematyar et al., 2025; Meng et al., 2026; Sidira et al., 2024). The synergistic effects of multiple stressors can increase deterioration, but thresholds are not known. It is likely

that genetic differences in muscle physiology and hypoxia tolerance are important modifiers that should be studied further.

6 Implications for seafood quality and human nutrition

6.1 Changes in protein quality and digestibility

The consumption of microplastic causes oxidative stress which leads to changes in protein structure and metabolic homeostasis, and this may have implications for the quality of tissues and digestibility. Polypropylene MPs result in an increase in ubiquitin conjugates and malondialdehyde, which suggest an increase in oxidative damage and a targeting of proteins for degradation by the proteasome. The simultaneous deficiency of amino acid precursors indicates that protein production is impaired, and so is oxidative fragmentation. They may affect the nutritive value of proteins and digestibility (Huang et al., 2025; Jeyavani et al., 2023). The digestibility can also decrease as a result of oxidative modification of residues such as cysteine and methionine; however, this has not been confirmed in aquatic systems exposed to MP (Kadac-Czapska et al., 2024; Lee et al., 2023; Soladoye et al., 2015). Proteolysis in response to stress is reflected by tissue specific responses such as depletion of metabolites in the liver and accumulation of amino acids in the gills, not by an

TABLE 2 Summary of microplastic-induced biological effects in teleost fish and their hypothesized relevance to heme proteins.

Biological level	Functional disturbance	Biomarker	Quantitative evidence	Mechanistic interpretation	Evidence	Potential heme protein relevance	Physiological impact	References
Gill epithelium or Respiratory interface	Impaired gas exchange and epithelial integrity	Histopathology, IL-1 β , TNF- α , MP retention	Gill microplastic prevalence reached up to 37%	Physical obstruction leading to ROS generation and inflammation	Proven	Hypothesized contribution to systemic oxidative load	Reduced oxygen uptake and increased risk of hypoxia	Li et al. (2025), Zheng et al. (2024)
Hepatopancreas or Liver	Disrupted detoxification and metabolic homeostasis	AKP, AST, ALT, LDH, GRP78, PERK, ATF4	AST and ALT levels increased in a dose-dependent manner; UPR marker expression increased	ROS-induced endoplasmic reticulum stress and inflammation	Proven	Hypothesized indirect effects on heme-related metabolism	Impaired metabolic flexibility	Cui et al. (2024), Das et al. (2025)
Systemic circulation or Hematology	Altered erythrocyte homeostasis	RBC count, Hb, PCV, MCHC, WBC	RBC count, hemoglobin concentration, and PCV decreased in some studies	Oxidative membrane damage	Proven (partial)	Hypothesized impact on oxygen-carrying capacity	Potential reduction in blood oxygen transport	Das et al. (2025), Rashid et al. (2025)
Skeletal muscle	Oxidative modification of structural proteins	Protein carbonyls, ubiquitin, muscle MDA	Protein carbonyl levels increased by 1.8–2.4-fold, whereas ubiquitin levels increased by 2–3-fold	ROS-mediated protein oxidation	Proven	Hypothesized myoglobin destabilization	Potentially accelerated post-harvest discoloration	Bobori et al. (2022), Yang et al. (2024)
Mitochondrial compartment	Compromised oxidative phosphorylation and metabolism	PPAR γ , FABP1, SCD1, amino acids	PPAR γ expression increased by 2.1-fold, whereas tryptophan and tyrosine levels decreased (1.35–1.66 log ₂ -fold)	Endoplasmic reticulum stress and metabolic disruption	Proven (metabolomics)	Hypothesized indirect effects on heme biosynthesis	Reduced metabolic efficiency	Cui et al. (2024), Xing et al. (2023)
Antioxidant defense system	Depletion of ROS-scavenging capacity	SOD, CAT, GPx; TAC	SOD, CAT, and GPx activities decreased by 38%–52%	Overwhelming of antioxidant defense systems	Proven	Hypothesized increased vulnerability of heme iron to oxidation	Systemic oxidative vulnerability	Das et al. (2025)
Gastrointestinal tract, Nutrient assimilation	Villi atrophy and impaired nutrient absorption	Histomorphological index, ADC	Dose-dependent villus atrophy was observed	Physical abrasion and tight junction disruption	Proven	Hypothesized reduction in amino acid availability for hemoprotein synthesis	Reduced growth performance	Lei et al. (2018), Rashid et al. (2025)
Proteostasis network	Imbalance in protein folding and degradation	LC3II, ATG, ubiquitin conjugates	LC3II and ubiquitin conjugate levels increased	Endoplasmic reticulum stress-induced autophagy	Proven	Hypothesized potential loss of functional hemoglobin and myoglobin pools	Proteostatic stress	Bobori et al. (2022), Cui et al. (2024)
Particle size-dependent toxicity	Enhanced nanoplastic uptake and systemic distribution	Tissue distribution and translocation	Nanoplastics exhibited greater tissue penetration and translocation than microplastics	Endocytic uptake and protein corona formation	Proven	Hypothesized direct intracellular interactions with hemoproteins	Higher systemic oxidative burden	Das et al. (2025), Pitt et al. (2018)
Post-harvest seafood quality	Oxidative deterioration	Protein carbonyls, MDA	Protein carbonyl levels increased by 1.8–2.4-fold	ROS-mediated protein oxidation	Proven	Hypothesized metmyoglobin formation and reduced heme iron bioavailability	Potential reduction in shelf-life and consumer acceptance	Bobori et al. (2022)

TABLE 3 Translational implications for seafood quality and human health.

Translational domain	Observed change in fish	Quantitative evidence	Evidence level	Potential seafood quality impact	Human health relevance	References
Oxidative stress in muscle	Protein carbonylation, MDA	Protein carbonyl levels increased by 1.8–2.4-fold, whereas MDA levels increased	Proven	Potentially accelerated post-harvest discoloration	Hypothesized reduction in heme iron bioavailability	Bobori et al. (2022) , Das et al. (2025)
Antioxidant capacity	SOD, CAT, GPx depletion	SOD, CAT, and GPx activities decreased by 38%–52%	Proven	Increased oxidative deterioration during storage	Hypothesized contribution to oxidative stress in consumers	Das et al. (2025)
Metabolic and amino acid profile	Tryptophan, Tyrosine depletion	Tryptophan and tyrosine levels decreased by 1.35–1.66 log ₂ -fold	Proven	Possible alteration of the nutritional amino acid profile	Unconfirmed impact on protein quality	Xing et al. (2023)
Intestinal barrier and inflammation	Villi atrophy, ER stress	GRP78, PERK, and ATF4 expression increased	Proven	Impaired nutrient absorption	Possible effects on intestinal barrier integrity	Cui et al. (2024) , Lei et al. (2018)
Contaminant vector	Adsorption of metals and persistent organic pollutants (POPs)	Metals were detected on the surface of microplastics	Proven	Potential increase in lipid oxidation and rancidity	Hypothesized amplification of contaminant exposure	Alberghini et al. (2022) , Hou et al. (2023)
Mitigation strategy	Microencapsulated astaxanthin	Significant reduction in ROS production and microplastic uptake	Proven	Potential improvement in color stability and shelf-life	Promising nutraceutical intervention	Zarantonello et al. (2024)

improved nutritional status. Despite the consistent oxidative markers, there is no study directly relating protein carbonylation and/or ubiquitination to measurable digestibility outcomes in fish muscle, and so a gap in nutritional risk assessment.

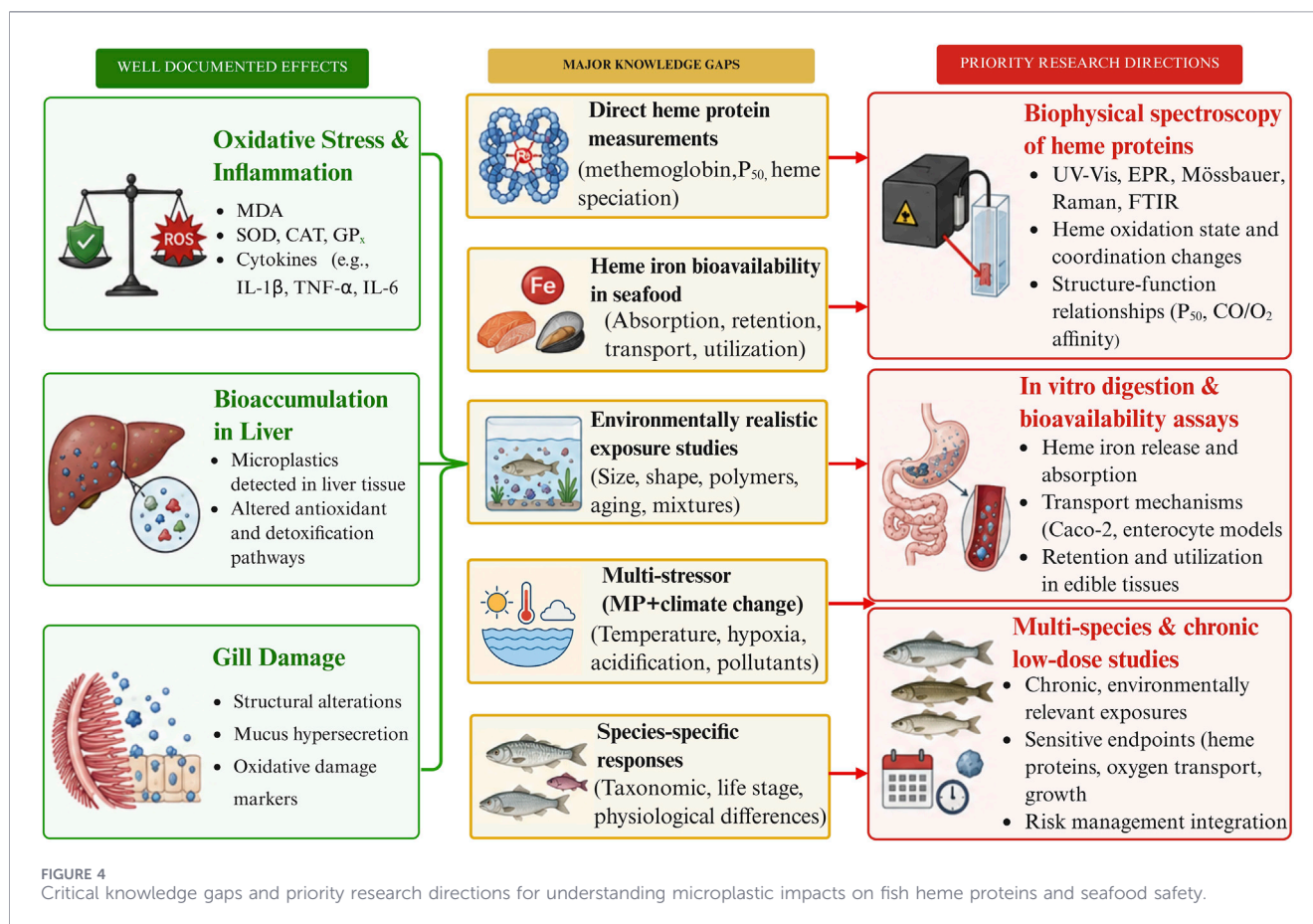
6.2 Impact on heme iron bioavailability

The bio-availability of heme iron is much greater in fish, and its effect on microplastic exposure has yet to be quantified. Current evidences indicates that microplastics cause oxidative stress, leading to increased malondialdehyde and protein carbonylation which can release heme iron from the hemoproteins, to less bioavailable non-heme forms ([Subaramaniyam et al., 2023](#)). The simultaneous depletion of major precursors (tryptophan, nicotinic acid) also indicates a compromised heme synthesis and structural instability, but no direct measurement of iron speciation or absorption is present. Secondary evidence suggests that mammalian models reduce Fe absorption by disrupting the intestinal lining, which has not been tested in aquatic systems. The effects can be exacerbated by additional competition for adsorption onto microplastics (Cd, Pb, Cu, Zn, Hg) and by Fenton-like reactions ([Alberghini et al., 2022](#); [Lusher et al., 2020](#)). Meanwhile heme iron absorption (~20%) is much higher than non-heme (2%–5%) then oxidative conversion could decrease nutritional value. The absence of models for digestion and uptake in the system, however, results in the inability to perform

quantitative risk assessment and the uncertainty of the effects on human iron bioavailability ([Kalman et al., 2025](#); [Piskin et al., 2022](#)).

6.3 Seafood safety concerns

The ingestion of microplastics through aquatic organisms, into the human body, is a new seafood safety issue as shown in [Table 3](#). Evisceration does not completely prevent exposure, as detected in edible tissues of fish, especially if particles translocate beyond the gut. Ingested microplastics can interact with intestinal epithelia, trigger oxidative stress and trigger the release of contaminants into the circulation ([Alberghini et al., 2022](#)). The compounds found on these particles include bisphenol A (5–200 ng/g), nonylphenol, PAHs, and metals (Cu 7.7 µg/g, Zn 290 µg/g, Pb 10.3 µg/g) that may be released during digestion ([Hou et al., 2023](#)). The current estimate of low direct chemical exposure fails to account for potential synergistic effects and oxidative stress and degraded proteins. Autophagy, apoptosis and metabolic disruption have been observed in fish exposed to microplastics, but these effects are yet to be translated to human health outcomes. There is evidence suggesting that smaller particles are more toxic and induce a greater inflammatory response ([Banaee et al., 2025](#); [Ghosh, 2025](#)). However, risk frameworks are still disjointed looking at particles, contaminants, nutritional degradation, separately which delays a proper assessment of cumulative dietary risk.



7 Critical knowledge gaps and future research directions

7.1 Lack of direct mechanistic studies on heme proteins

The reported increases in MDA and decreases in SOD, CAT and GPx are generic and occur under many oxidative stressors. They have no specific data for heme protein structure, heme iron redox state (Fe²⁺ to Fe³⁺), globin stability or oxygen-binding parameters. There are no studies to measure levels of methemoglobin, P₅₀ value, or conduct spectroscopic analysis of heme coordination in microplastic-exposed fish. Therefore, the relation between oxidative stress and heme protein dysfunctions is still speculative.

7.2 Limitations in experimental design and ecological relevance

A large portion of the laboratory experiments are based on relatively high concentrations of pristine polystyrene or polypropylene particles that do not accurately represent the environmentally relevant complex, weathered, and heterogeneous microplastics. There is also strong dependence on a small number of model species, which restricts the scope of generality across the range of fish species that have various hemoglobin isoforms and hypoxic tolerance. The results of many findings have only limited translational value because of these design decisions.

7.3 Translational and interdisciplinary gaps

Many differences exist between the molecular level observations and the higher order results, including oxygen transport capacity, post-harvest muscle quality, and nutritional value of seafood. The possible effect of the changes in the bioavailability of heme iron has never been evaluated. These gaps need to be filled with integrated approaches that include realistic exposure scenarios, *in vitro* digestion models, and a biophysical heme analysis.

7.4 Multi-stressor and standardization needs

Few data is available about the interactions between microplastics and other climate-related stressors such as hypoxia and increased temperature. There is an urgent need for studies to be reproducible and comparable, due to the lack of particle characterization, exposure regimes and reporting standards.

7.5 Implications under climate change scenarios

The combined effect of climate stressors with microplastic exposure is not well understood. Hypoxia, high temperature and MPs independently affect oxygen metabolism, but the combined effects of these factors with MPs are not widely studied. With increasing temperature, uptake of oxygen may increase due to metabolism, and the rate of oxidation may increase, which could exacerbate MP effects on

heme proteins. But there is a lack of studies that directly measure interactive effects on oxygen equilibrium curves or tissue hypoxia thresholds. Lack of multi-stressor frameworks is a significant constraint. Further studies should have factorial designs combining the variables of temperature, dissolved oxygen, and MP exposure. When combined with real-time hemoglobin spectroscopy, this approach will help determine how climate stress increases the vulnerability of heme proteins.

7.6 Translational research for seafood systems

There is a considerable disconnect between aquatic toxicology and human nutrition studies, as can be seen in [Figure 4](#). Although there are no direct data to prove it, oxidative stress may affect the heme iron concentration, digestibility, and bioavailability in seafood. Integrated studies that consider possible interactions between microplastic exposure, protein oxidation and micronutrient availability are needed. To resolve these uncertainties, *in vitro* gastrointestinal digestion models, standardized for the specific purpose of heme speciation, would be advantageous, along with the monitoring of the appropriate biomarkers (serum ferritin) during the digestion process.

8 Conclusion

The current evidence indicates that microplastics regularly cause oxidative stress, inflammation, and metabolic disruption in teleost fish. These responses create a pro-oxidant cellular environment which can make heme-containing proteins like hemoglobin and myoglobin more susceptible. At present, however, there are no direct data on the role of microplastic-induced heme protein dysfunction such as methemoglobin formation, alteration of the oxygen-binding affinity (P_{50}), and myoglobin oxidation. Conclusions in the field are still largely based on generic oxidative stress biomarkers without specific measurements of heme structure/function. This critical review emphasizes the large discrepancy between the known general toxicity and the suspected effects on the transport of oxygen and the nutritional quality of seafood. To overcome the limitations in the current studies, exposure concentrations are unrealistically high, species diversity is limited, and there has been an overrepresentation of pristine particles. Source reduction of plastic pollution is a key priority to protect aquatic ecosystems and global food security.

Author contributions

NA: Writing – original draft. ND-a: Writing – review and editing. KK: Writing – review and editing. MN: Supervision,

Writing – original draft, Writing – review and editing. MQ: Writing – review and editing. CJ: Writing – review and editing. FH: Writing – review and editing.

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Conflict of interest

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