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Review

Marine-Derived Antioxidant Peptides as Pharmaceutical and Nutraceutical Candidates

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Abstract

This review examines the sources, sequence–activity relationships, mechanisms, and translational status of marine antioxidant peptides, in view of the regulatory reassessment of synthetic antioxidant additives. PubMed/MEDLINE, Scopus, and Web of Science were searched for reports supplying a defined sequence and quantified antioxidant activity; the most active peptide of the most recent qualifying report was retained per source species. Peptides derive mainly from hydrolyzed fish, invertebrate, and algal proteins, largely from processing by-products. Aromatic and sulfur-containing residues, hydrophobicity, and residue position recur among the most potent sequences only as tendencies: three of twenty tabulated marine sequences carry neither residue type, and chain length shows no consistent relationship with potency in this non-representative set. Activity is attributed to radical neutralization, metal chelation, and an indirect Keap1-Nrf2 route. For defined sequences, evidence diminishes from cell-free assays to whole organisms: of twenty-three marine entries, one reaches a whole organism, two non-marine comparators being excluded. Nine in vivo studies, seven in animals and two in humans, are tabulated in parallel, but six test hydrolysates or multi-component preparations outside the sequence-level criteria. No tabulated peptide has been compared with a synthetic antioxidant in a product matrix. Non-standardized assays, predictive models trained on non-marine data, and unreported allergen and heavy-metal risks remain the principal barriers.

Keywords: marine peptide; antioxidant activity; oxidative stress; sequence–activity relationship; Keap1-Nrf2 pathway; nutraceutical; drug discovery; enzymatic hydrolysis; machine learning

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Academic Editors: Daniel Carneiro Moreira and José Roberto de Souza de Almeida Leite

Received: 4 November 2026
Revised: 21 November 2026
Accepted: 23 November 2026
Published: 26 November 2026

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1. Introduction

Oxidative stress arises when the generation of reactive oxygen species (ROS) exceeds the capacity of an organism or a formulation to neutralize them, resulting in cumulative damage to lipids, proteins, and nucleic acids [1,2]. In biological systems, this imbalance is implicated in aging and a broad spectrum of chronic diseases; in lipid-containing products, it manifests as lipid peroxidation, generating aldehydes and other secondary products

responsible for rancidity and the loss of nutritional and functional quality [3]. Pharmaceutical, nutraceutical, and food manufacturers have therefore relied on antioxidant additives for decades to delay this process.

This function has traditionally been fulfilled by synthetic phenolic compounds, chiefly butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and tert-butylhydroquinone (TBHQ), which remain widely used for their low cost, efficacy, and ease of formulation. In the United States, BHA and BHT are generally recognized as safe for use as chemical preservatives, on the condition that the total antioxidant content does not exceed 0.02% of the fat or oil content of the food, and are separately authorized as direct food additives in named foods at limits expressed in parts per million of the food itself, ranging for BHA from 2 ppm in beverages and desserts prepared from dry mixes to 1000 ppm in active dry yeast, and for BHT from 10 to 200 ppm [4]. That position is under reassessment. Network toxicology analyses have predicted hepatic, renal, and neurological toxicity for the three compounds [5], although such analyses are computational and do not by themselves establish a hazard. In August 2025, the United States Food and Drug Administration added BHA and BHT to its list of chemicals in the food supply under agency review [6] and in 2026 issued requests for information on their uses and safety data, the comment period for BHT being subsequently reopened [7–9]. Reformulation pressure arising from preference for naturally derived preservatives [10] has directed manufacturers toward alternatives of comparable efficacy without the same regulatory uncertainty.

Plant phytochemicals, such as polyphenols, flavonoids, and terpenoids, have demonstrated antioxidant activity across diverse matrices and are increasingly proposed as replacements for synthetic phenolic additives [10]. Marine organisms, which are adapted to extreme and highly variable physicochemical conditions, produce peptides and proteins with structural and functional properties distinct from those of their terrestrial counterparts [11]. Marine-derived antioxidants have been proposed as therapeutic candidates for oxidative-stress-associated cardiovascular, metabolic, and neurodegenerative conditions [12].

Marine peptides are of particular interest to the pharmaceutical and nutraceutical sectors. Generated primarily by the enzymatic hydrolysis of proteins from fish, molluscs, crustaceans, echinoderms, algae, and cyanobacteria, they have demonstrated antioxidant capacity in vitro, and fish-derived hydrolysates and peptides have additionally been reported to support glucose management and muscle protein synthesis [13]. Marine organisms have therefore attracted attention as a largely underexploited source of novel bioactive compounds [14], with reported antibacterial, anti-inflammatory, antiaging, and skin-protective activities alongside antioxidant capacity [15]. Systematic toxicological evaluation, however, has not been reported for the peptides reviewed here: the available animal studies were designed to test efficacy, and the absence of marked adverse effects cannot substitute for a dedicated safety assessment.

The field nonetheless remains fragmented. Studies differ considerably in the species examined, the hydrolysis and purification protocols used, and the assays employed to quantify antioxidant activity, which hinders direct comparison of results and identification of the structural features that most reliably predict potency. This review consolidates current knowledge by outlining the principal marine sources and the enzymatic processes used to generate these peptides, synthesizing the available sequence data, summarizing the mechanisms through which these peptides act and the extent to which in vitro findings have been reproduced in vivo, and evaluating the prospects and remaining barriers to pharmaceutical and nutraceutical application. Two potential roles of these peptides should be distinguished, as each requires a different form of evidence: as technological antioxidants that protect a product against oxidative deterioration, for which direct comparison with synthetic additives within the product matrix is the relevant criterion, and as bioactive

ingredients with physiological effects, for which evidence from cell, animal, and human studies is required.

Existing reviews are organized either by source taxon and preparation route [16] or by structure–activity relationship [17–20]; the most recent also cover artificial-intelligence screening [21], and a parallel body of work covers marine collagen peptides [22]. The present review differs in four respects. Each sequence–activity report is annotated with the highest level at which its antioxidant claim was validated, whether cell-free assay, cultured cell, or whole organism, and the decline in supporting evidence across that gradient is treated as a substantive finding, not merely as a concluding caveat. Conventional and computational discovery routes are compared directly in Table 1 instead of being merged. Reported potencies are not converted to a common scale, and every entry is labeled as a purified or synthesized peptide or a characterized hydrolysate fraction, because the cross-study comparability that conversion implies does not exist in this literature. Finally, the accuracy figures reported for antioxidant peptide predictors are interpreted against the composition of the benchmark datasets on which they were obtained, which are predominantly non-marine.

2. Materials and Methods

2.1. Literature Search and Scope

Records were retrieved from PubMed/MEDLINE, Scopus, and the Web of Science Core Collection, covering January 2005 to September 2026. The window was set to the two decades over which sequence-level characterization of marine antioxidant peptides became routine; a small number of sequence-resolved reports predate it and were not included, so the tables below describe that window and not the field in its entirety. The search combined three concept blocks, namely marine source, antioxidant peptide, and preparation or characterization, joined by the AND operator, with truncation and phrase searching applied throughout. Reference lists of the retrieved reviews were hand-searched, and the search was re-run during manuscript preparation to capture newly published records.

Studies were within the scope of this review if they reported all three of the following: A peptide derived from a marine organism or a marine processing by-product; antioxidant activity reported quantitatively, whether as IC_{50}, EC_{50}, percentage scavenging, oxygen radical absorbance capacity (ORAC) or ferric reducing antioxidant power (FRAP), or as electron spin resonance (ESR) scavenging or inhibition of lipid peroxidation measured against a named reference antioxidant; and a defined amino acid sequence, either resolved experimentally or derived computationally and then confirmed by synthesis and assay. Excluded were non-peptide marine antioxidants such as polysaccharides, carotenoids, polyphenols, and sterols; endogenous tissue peptides not released by hydrolysis, such as carnosine and anserine; freshwater and terrestrial sources; reports offering only in silico prediction without experimental assay; and reviews, conference abstracts, and publications not available in English. Because the number of records at each screening stage was not recorded (Section 2.2), these three conditions are described here as the scope criteria delimiting the literature surveyed and not as the eligibility criteria of a systematic review; the sequence-level tables below are drawn from that literature but are not presented as the complete set of records satisfying the criteria. Seven tabulated entries depart from the criteria and are keyed (a) to (g) in the footnotes to Tables 2–4. A defined sequence is required because the subject of this review is the relationship between sequence and activity, which cannot be examined for preparations of unresolved composition. This requirement excludes most preparation-level in vivo work; that literature is therefore reported in parallel in Section 5.2, and the decline in supporting evidence described in this review refers to defined sequences and not to marine antioxidant preparations generally.

2.2. Synthesis Approach and Nomenclature

This was a structured search rather than a formal systematic review: it was not registered in a public protocol repository, screening was performed by a single reviewer, no risk-of-bias instrument was applied, and no quantitative synthesis was attempted. The absence of synthesis is deliberate, as potency is reported across incompatible assay formats and concentration units, so effect sizes cannot be pooled. Each report is instead labeled with the level at which its antioxidant claim was validated, and the compositional patterns reported below are described as recurring patterns, not as statistical associations. Literature falling outside these scope criteria is cited where relevant. Species are named as in the source study, with the currently accepted name in the World Register of Marine Species given alongside where the two differ, and algal names are checked additionally against AlgaeBase; reference titles are reproduced as published, so an outdated binomial appearing in a title is not amended. The tabulation of whole-organism studies also extends beyond these scope criteria, since several of the most informative such studies used hydrolysates or peptide complexes for which no single sequence was resolved; these are identified as preparations and not as defined peptides. Because the search was conducted iteratively, combining database queries with manual screening of reference lists and updated searches during manuscript preparation, and because only one representative entry per source species or material was retained in the tables, the number of records at each screening stage is not reported. The tables are therefore illustrative of the literature surveyed rather than exhaustive.

3. Marine Sources and Peptide Generation

3.1. Marine Sources

Marine antioxidant peptides have been reported from a broad range of taxa, most arising as by-products of existing seafood industries rather than from dedicated harvests [23]; such by-products have themselves been reviewed as a feedstock [16]. Fish processing waste, comprising skin, bone, scales, and viscera generated during filleting, is the most extensively studied source, and the purification and sequence characterization of peptides from it have been reviewed in detail [17]. Molluscs such as oysters, mussels, clams, and abalone constitute a second category, and crustacean shells and heads constitute a third, the latter notable for co-occurring chitin that complicates but does not preclude peptide recovery. Macroalgae form a fourth category, yielding amino acid profiles distinct from those of animal-derived counterparts; echinoderms, notably sea cucumber, form a smaller fifth [24]; and cyanobacterial and microalgal proteins such as C-phycocyanin form a sixth. Across all categories the peptides of interest are embedded within larger parent proteins and must be released before their antioxidant activity becomes measurable.

3.2. Enzymatic Hydrolysis and Purification

The conventional route to peptide release is enzymatic hydrolysis, the operating conditions, pre-treatments, and scale-up of which for fisheries by-products have been reviewed in detail [25]. Proteases such as Alcalase, Flavourzyme, pepsin, trypsin, papain, and Neutrase are applied individually or sequentially under controlled pH and temperature, and workflows combining Alcalase hydrolysis with ultrafiltration and reverse-phase high-performance liquid chromatography (HPLC) are well-documented in marine matrices [26]. Together with microbial fermentation, enzymatic hydrolysis is regarded as an effective means of obtaining bioactive hydrolysates from underutilized fish protein by-products, whereas chemical synthesis is used to produce peptides of defined sequence [27]; in enzymatic hydrolysis, the choice of protease markedly influences the outcome. For example, of six proteases applied separately to Nile tilapia skin gelatin, Flavourzyme, rather than

Alcalase, yielded the most active hydrolysate against 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radicals and lipid peroxidation [28]. Selection also varies with the tissue, so protocols optimized for fish skin are not directly transferable to viscera or mollusc muscle [18]. Crude hydrolysates are then fractionated by ultrafiltration, resolved by gel filtration and reverse-phase HPLC, and identified by tandem mass spectrometry.

This workflow has generated most of the sequence data reviewed below, but each round of hydrolysis, fractionation, and activity testing is time-consuming, and the activity of a given fraction can be confirmed only retrospectively. Screening of a new species or by-product therefore remains largely empirical.

3.3. Computational Prioritization of Candidate Sequences

This limitation has prompted the development of methods that predict antioxidant activity directly from an amino acid sequence before hydrolysis is performed [29]. AnOxPePred, a deep learning tool developed for this purpose, was among the first web-accessible predictors of peptide antioxidative potential, and machine learning has since become an established branch of bioactive peptide research [30]. Subsequent predictors have extended this approach in different directions: A bidirectional long short-term memory (LSTM) quantitative structure–activity model, AnOxPP, predicts activity from interpretable amino acid descriptors [31]; an ensemble learner, iAnOxPep, removed the peptide-length restrictions that constrained earlier tools [32]; and a multi-view architecture integrating sequence embeddings with molecular-graph features reports accuracies of 0.97 and 0.90 on two of the three standard antioxidant peptide benchmarks and 0.80 on the third [33]. Those benchmarks, AnOxPePred, AnOxPP and AOPP, are drawn from BIOPEP-UWM, DFBP, the Antimicrobial Peptide Database, PlantPepDB and FermFooDB and comprise roughly 1400 to 3000 sequences each; none is marine-specific, and plant- and fermented-food-derived peptides are represented explicitly.

The same approach has been applied to marine organisms. In one study, the mucus proteome of the oyster *Crassostrea gigas*, currently *Magallana gigas*, was sequenced, and approximately 43,000 candidate fragments were generated computationally; a machine learning model then selected those likely to be bioactive, and six candidates were validated experimentally [34]. The study targeted antimicrobial rather than antioxidant activity but demonstrates the workflow on a marine proteome: undirected hydrolysis screening is replaced by a targeted candidate list generated in silico. An LSTM model has been trained to predict angiotensin-converting-enzyme-inhibitory potency from sequence alone [35], and ensemble deep learning frameworks predict bioactive peptides more generally [36]. Frameworks coupling deep learning to quantum-chemical calculation have extended prediction to experimental confirmation: ten peptides prioritized in this way were synthesized and assayed, with LLA showing the highest 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ABTS scavenging, at 0.108 and 0.437 mmol/g, although its DPPH figure remained marginally below that of glutathione [37]. Considered alongside reviews describing artificial intelligence as a tool for uncovering bioactive peptides in food-derived proteins [38], these developments indicate a hybrid model in which computational prediction prioritizes candidates and targeted extraction and assay-based confirmation follow.

The two discovery routes are compared in Table 1, which records the method, the reported outcome, and the extent of experimental confirmation for representative studies of each type.

Table 1. Comparison of discovery routes: conventional extraction versus computational prioritization.

Source	Route	Method or Model	Key Outcome	Target and Status	Ref.
Mackerel (*P. japonicus*, currently *S. japonicus*)	Classical	Hydrolysis, column chromatography, LC-MS/MS	Fourteen sequences resolved in the most active fraction	Antioxidant; sequences resolved and assayed	[39]
Blue mussel (*M. edulis*)	Classical	Microbial protease hydrolysis, ultrafiltration, gel chromatography, LC-MS/MS	Five bioactive peptides identified and subjected to molecular docking	Antioxidant; peptides identified and assayed	[40]
Antarctic krill (*E. superba*)	Classical	Alcalase hydrolysis, ultrafiltration, chromatography, ESI-MS	Fifteen candidate peptides purified and sequenced	Antioxidant; peptides purified and assayed	[41]
Abalone (*H. discus hannai*)	Computational	Virtual enzymatic hydrolysis to a 363-peptide library; Keap1 docking	Ten peptides ranked by Keap1 docking score; DEDEDEDK, lowest of the ten on that score, was the most active in HUVECs	Antioxidant; cell assay performed, Keap1 binding predicted only	[42]
Oyster (*C. gigas*, currently *M. gigas*) mucus proteome	Computational	Proteome sequencing with machine learning prioritization of ~43,000 candidate fragments	Six candidates validated in vitro; antimicrobial target, workflow transferable	Antimicrobial, not antioxidant; candidates validated in vitro	[34]
General tool	Computational	AnOxPePred deep learning predictor	Predicts antioxidative potential from sequence before hydrolysis	Antioxidant; computational prediction tool	[29]
General tool	Computational	iAnOxPep ensemble classifier	Removes the peptide-length restrictions of earlier predictors	Antioxidant; computational prediction tool	[32]
General tool	Computational	Deep generative model with DFT calculations	Twelve peptides designed; six synthesized, all active in the DPPH assay but giving suboptimal results against hydroxyl radicals	Antioxidant; designed peptides synthesized and assayed	[43]
Sea cucumber (*Holothuria tubulosa*)	Computational	Proteomic data combined with bioinformatic activity prediction	Forty top-ranked antioxidant and anti-inflammatory peptides identified by docking and molecular dynamics; experimental validation pending	Antioxidant and anti-inflammatory; prediction only, experimental validation pending	[44]

Table 1. *Cont.*

Source	Route	Method or Model	Key Outcome	Target and Status	Ref.
General tool	Computational plus experimental	Bi-LSTM predictor with quantum-chemistry descriptors	Ten prioritized peptides synthesized and assayed; LLA most active	Antioxidant; prioritized peptides synthesized and assayed	[37]

LC-MS/MS = liquid chromatography–tandem mass spectrometry; ESI-MS = electrospray ionization mass spectrometry; DFT = density functional theory; Bi-LSTM = bidirectional long short-term memory; HUVEC = human umbilical vein endothelial cell; DPPH = 2,2-diphenyl-1-picrylhydrazyl; Keap1 = Kelch-like ECH-associated protein 1. Table 1 illustrates discovery routes and is not confined to the scope criteria defined in the Methods: the sea cucumber entry awaits experimental validation, and the oyster mucus entry targeted antimicrobial, not antioxidant, activity, both being retained because they demonstrate the computational workflow on a marine proteome. The target of each study and the extent of its experimental confirmation are stated in the Target and Status column.

4. Sequence–Activity Relationships

Enzymatic hydrolysis explains how peptides are released but not why some fragments scavenge radicals considerably more effectively than others. Comparison of sequences across studies reveals compositional patterns consistent with recent structure–activity reviews of marine peptides [19,20]. These are described here as sequence–activity relationships, because the underlying reports supply a primary sequence, not a resolved three-dimensional structure.

The first pattern concerns hydrophobicity, and the evidence for it is mixed. Fish skin gelatin is unusually rich in glycine, proline, alanine, and hydroxyproline, and gelatin-derived hydrolysates recur among the more active antioxidant fractions reported; in thornback ray skin gelatin, by contrast, hydrophobic peptide content did not order the hydrolysates by radical-scavenging activity, and the activity of the most potent preparation was attributed instead to its higher combined histidine, tyrosine, methionine, and phenylalanine content: 13.22% of residues against 10.57% in the least active hydrolysate [45]. Hydrophobic residues are thought to improve access to lipid–water interfaces, where peptides interact more readily with lipid-soluble radicals, while histidine and acidic residues may contribute to the chelation of pro-oxidant transition metal ions [18]. Gelatin and scale collagen from other species behave comparably, with antioxidant peptides recovered from skipjack tuna scale gelatin [46] and large yellow croaker (*Pseudosciaena crocea*, currently *Larimichthys crocea*) scales [47]. Interpretable machine learning analyses implicate the same residues: SHapley Additive exPlanations (SHAP) attribution over the amino acid composition features of a classifier within a multimodal antioxidant peptide framework identified proline, leucine, alanine, tyrosine, and glycine as the strongest contributors to a positive prediction [48]. The same attribution assigned negative weight to methionine, cysteine, and tryptophan, which appears inconsistent with the sulfur-containing and aromatic residues discussed below; this most plausibly reflects how the training data were constructed rather than the underlying chemistry: the model was trained on a general antioxidant peptide database that is not marine-specific paired with length-matched negative sequences generated computationally instead of being shown experimentally to be inactive, and a negative set assembled that way transfers its own compositional bias directly into the attribution.

A second pattern involves aromatic residues. Tyrosine and tryptophan can transfer a hydrogen atom from their phenolic hydroxyl and indole N–H groups, respectively, to a radical, and the resulting peptide-derived radical is stabilized by resonance delocalization over the aromatic ring. Phenylalanine lacks a comparably labile hydrogen, whereas histidine acts chiefly through its imidazole ring, which also coordinates metal ions. Molecular docking of antioxidant peptides from tilapia skin supports the contribution of aromatic residues only

in part, identifying tyrosine alongside the non-aromatic proline and alanine as the residues most responsible for radical scavenging [49]; aromaticity is therefore one contributor among several and not the sole determinant. The pattern nonetheless recurs across highly active marine peptides with confirmed sequences: the oyster (*Crassostrea rivularis*, currently *Magallana rivularis*) heptapeptide YAKRCFR pairs an N-terminal tyrosine with a C-terminal arginine [50], a salmon skin collagen peptide terminates in the aromatic-rich motif YHY [51], and the tripeptide YLL from the red alga *Eucheuma cottonii* (currently *Kappaphycus alvarezii*) protected endothelial cells in an effect attributed partly to its tyrosine residue [52]; the corresponding potencies are tabulated below. Sulfur-containing residues contribute through a parallel route: cysteine donates the hydrogen of its thiol side chain, while the thioether sulfur of methionine is readily oxidized to the sulfoxide, and both therefore quench radicals without an aromatic ring [53]. The salmon collagen peptide above supplies a direct instance: its methionine was detected in the oxidized form, and the source proposes that residue as the active site [51]. The most abundant peptide in the most active fraction of a mackerel (*Pneumatophorus japonicus*, currently *Scomber japonicus*) hydrolysate, QCCCFT, contains three consecutive cysteines and accounted for 42.05% of that fraction by chromatographic peak area; of the fraction's 14 synthesized sequences, it was the most active across DPPH, ABTS, and hydroxyl radical assays [39]. Three adjacent free thiols are, however, readily lost to air oxidation and to intermolecular disulfide formation, and neither the storage nor the digestive stability of this sequence was examined, so its in-solution potency should not be assumed to persist under physiological conditions. Aromatic and basic residues also recur together: the skin hydrolysates of horse mackerel (*Megalaspis cordyla*, published as *Magalaspis cordyla*) and croaker (*Otolithes ruber*) yielded NHRYDR and GNRGFACRHA, both inhibiting polyunsaturated fatty acid peroxidation more effectively than α-tocopherol [54]. Residue position also bears on activity: of five peptides from *Mytilus edulis* hydrolyzed with a marine *Bacillus velezensis* protease, the one with a C-terminal tyrosine was the most active even though its hydrophobic residue content, at 37.5%, was the second lowest of the five and well below the 59.9% of the most hydrophobic [40]. Earlier work on the same species reported YPPAK [55] and an octapeptide whose sequence is given inconsistently in its source: the abstract and body text of [56] read PIIVYWK, whereas the table reporting the activities of the synthesized peptides in the same report reads PIISVYWK. The reported mass of 1004.57 Da agrees with the calculated monoisotopic mass of PIISVYWK (1004.57 Da) rather than that of PIIVYWK (917.54 Da), and the same group refers to the peptide as the octapeptide PIISVYWK in later work [57]. The sequence is therefore taken to be PIISVYWK; only the most recent report is tabulated.

Chain length differs from the two patterns above in that it shows no consistent relationship with potency across the set tabulated here. In the red algal hydrolysate, the two dipeptides among six isolated peptides, TA and MN, were the weakest radical scavengers, with DPPH EC_{50} values of 8.96 and 3.57 mM against 0.52 mM for the tripeptide YLL, but they were not inactive, and the tetrapeptide YSKT was in turn weaker than that tripeptide [52]. Short chains are therefore not excluded from activity as a class. Beyond the dipeptide range, no ordering by length is apparent either. In blood cockle (*Tegillarca granosa*) hydrolysate, the tetrapeptide WPPD was more potent than the longer MDLFTE in every assay applied [58], while the pentapeptide LANAK scavenged DPPH more effectively, at 83.8%, than either of the two longer sequences it was ranked against among seven peptides purified from *Saccostrea cucullata* hydrolysate, a ten-residue peptide at 76.6% and a fourteen-residue peptide at 75.5% [59]. The most potent entries in the tables below range from three to ten residues without a discernible trend, and interpretable attribution points the same way without bearing on length directly: the SHAP analysis described above ranks individual residues by their contribution to a positive prediction and does not treat chain length as a variable at all [48]. Residue identity and

placement therefore appear to matter more than chain length does. These observations describe the sequences retained in Tables 2–4 and the studies from which they are drawn. Because one entry per species was retained and that entry is the most active sequence of its study, the set is not a sample of marine antioxidant peptides as a class, and no general absence of a relationship between chain length and antioxidant activity should be inferred from it.

Two qualifications should be attached to these compositional patterns, both visible within the tables themselves. First, the patterns are tendencies rather than requirements: of the twenty marine single sequences tabulated below as the leading entry for their source species or material, three carry no aromatic residue, namely LANAK, DEDEDEDK and the seahorse tripeptide AGD, and none of the three contains a sulfur-containing residue; the freshwater comparator KAPDPGPGPM, listed separately at the foot of Table 2, also lacks an aromatic residue. Second, the most striking of these, the abalone octapeptide DEDEDEDK, is composed entirely of acidic residues and a single lysine and has no side chain that readily donates a hydrogen atom, yet it was the most active among ten candidates ranked by docking score against Kelch-like ECH-associated protein 1 (Keap1), despite ranking last of the ten on that score; its activity was attributed to competitive occupancy of the Kelch domain of Keap1 [42]. That attribution rests on docking rather than on a binding measurement, and the authors of the primary report describe it as requiring validation. Neither radical scavenging nor metal chelation was assayed in that study, so although the seven carboxylate side chains would be expected to coordinate transition metals by the criteria set out below, no evidence bears on the question either way. Its activity therefore cannot be explained by hydrogen-donating capacity alone and is discussed further under the indirect mechanism below.

One comparison should nonetheless be avoided. A crude hydrolysate is quantified as total hydrolysate mass, of which the active sequences are only a fraction, and its IC_{50} is therefore not comparable on a mass basis with that of a purified peptide. The DPPH IC_{50} of 6.7 mg/mL reported for a shrimp shell waste hydrolysate composed mainly of peptides below 4 kDa [60] reflects dilution by inactive fragments as much as any property of the sequences it contains. The converse also occurs: the thornback ray hydrolysate tabulated below records a lower nominal IC_{50} than two of the single peptides, which indicates that the two quantities cannot be ranked against each other in either direction.

IC_{50} values in the literature are reported in inconsistent units: milligrams of crude hydrolysate per milliliter in some studies, micrograms of a single purified peptide per milliliter in others, and micromolar concentrations elsewhere. Cross-study comparisons should therefore be regarded as indicative only, unless both potency and purity are reported together.

The three tables that follow are drawn from the literature surveyed and apply one further reduction rule: one entry per source species or, where the source study resolved none, per source material, namely the most potent peptide reported for it or, where a study did not rank its peptides against one another, one of those it identified as most active; where a species was covered by more than one qualifying study, the most recent report supplying both a full sequence and a reported activity is used. Each entry is therefore the most active sequence of the single study retained for that species or material, which is not the same as the most active sequence obtainable from that source: A more potent sequence may exist in an earlier report, in a study not retained, or among sequences that no study has yet resolved. Retaining one entry per species also sets aside the less active sequences reported alongside it, so the compositional patterns described in Section 4 are drawn from the upper end of each study's range and should not be read as a survey of marine antioxidant peptides generally. Seven entries depart from the scope criteria and are keyed in the footnotes to Tables 2–4, so that each departure can be identified in the row to which it applies: (a) thornback ray and (b) shrimp shell, where the quoted potency is that of the unfractionated hydrolysate rather than of any resolved sequence; (c) green mussel and (d) Alaska pollock, where sequences

were resolved but the reported potency belongs to the whole hydrolysate or purified fraction and not to a single peptide; (e) oyster (*Saccostrea cucullata*), where the source reports a scavenging percentage for the purified peptides without stating the concentration at which it was measured, meaning that the value supports only a within-study ranking; and (f) Nile tilapia and (g) C-phycocyanin, which depart with respect to origin rather than potency, the first being a freshwater fish and the second a cyanobacterium cultivated in inland waters. Entries (f) and (g) are placed at the foot of their tables, identified as comparators, and excluded from every count reported in this review. Potency itself is reported at three levels across the set, and the tables distinguish them: A numeric value for the isolated peptide; a numeric value for the hydrolysate or fraction from which it was resolved; and, for one entry, effects recorded at defined test concentrations with no potency value of any kind. Each row also records the highest level at which the antioxidant claim was validated. Fish-derived sequences are collected in Table 2 and mollusc-derived sequences in Table 3. Crustacean, echinoderm, algal, and cyanobacterial sequences are collected together in Table 4, because each of these groups yields markedly fewer qualifying records; that imbalance reflects where characterization remains sparse, not where activity is absent.

Table 2. Representative antioxidant peptides from fish sources.

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
Thornback ray (*Raja clavata*) skin (a)	TRGH-A26, crude hydrolysate	Mixed	DPPH IC50 1.98 mg/mL, with BHA as positive control [45]	Cell-free
Salmon (species not specified) skin collagen	PMRGGGGYHY, synthesized	1094.2 calculated; no mass reported	ORAC 2.51 ± 0.14 mmol TE/g for the synthesized peptide; the remaining results in this cell are for the parent fraction, not the peptide, which made up more than 86% of the parent fraction F5; that fraction scavenged DPPH 73.29 ± 1.03% and hydroxyl radicals 72.73 ± 3.34%, protected plasmid DNA and reduced intracellular ROS in HUVECs [51]	Cell-free
Miiuy croaker (*Miichthys miiuy*) swim bladder	FPYLRH, synthesized	~832	DPPH EC_{50} 0.51 mg/mL; hydroxyl radical EC_{50} 0.68 mg/mL; superoxide EC_{50} 0.34 mg/mL [61]; protective in H_2O_2-damaged HUVECs [62]	Cell culture (HUVEC)
Hoki (*Johnius belengerii*) skin gelatin	HGPLGPL, purified	797 as reported	Superoxide, carbon-centered and DPPH radical scavenging by ESR of 97.65 ± 0.43%, 95.12 ± 0.85% and 80.09 ± 0.31%, with 23 µg/mL required to halve the superoxide signal; linoleic acid peroxidation inhibited more than by α-tocopherol and close to BHT; SOD, GSH-Px and CAT activities elevated in Hep3B cells at 150 µg/mL [63]	Cell culture (Hep3B)
Skipjack tuna (*Katsuwonus pelamis*) scale gelatin	DGPKGH, purified	~610	EC_{50} 0.54 mg/mL against DPPH, 0.41 mg/mL against hydroxyl and 0.71 mg/mL against superoxide radicals, the lowest of the three isolated peptides on all three [46]	Cell-free
Alaska pollock (*Theragra chalcogramma*, currently *Gadus chalcogrammus*) skin collagen (d)	Fraction A1a3c-p; four sequences resolved (YGCC, DSSCSG, PAGNVR, NNAEYYK)	444–900 (resolved peptides)	Hydroxyl radical IC_{50} 7.63 µg/mL for the fraction; activity rose through two rounds of simulated GI digestion [64]	Cell-free (fraction-level potency)

Table 2. *Cont.*

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
Mackerel (*Pneumatophorus japonicus*, currently *Scomber japonicus*)	QCCCFT, synthesized	~704	42.05% of the most active fraction by peak area; most active of the 14 synthesized sequences on DPPH, ABTS and hydroxyl radicals; Keap1 binding predicted by docking; protected HepG2 cells from H_2O_2 damage [39]	Cell culture (HepG2)
Horse mackerel (*Megalaspis cordyla*) skin	NHRYDR, purified	856	DPPH 72.3 ± 2.5% and hydroxyl radical 51.2 ± 2.3% scavenging by ESR at 1 mg/mL; PUFA peroxidation inhibited more than by α-tocopherol [54]	Cell-free
Croaker (*Otolithes ruber*) skin	GNRGFACRHA, purified	1101.5 as reported	DPPH 79.6 ± 2.6% and hydroxyl radical 56.8 ± 2.1% scavenging by ESR at 1 mg/mL; PUFA peroxidation inhibited more than by α-tocopherol [54]	Cell-free
Big-belly seahorse (*Hippocampus abdominalis*), farmed whole animal	AGD, purified	262.1	Peroxyl radical scavenging by ESR, IC_{50} 0.18 mg/mL for the purified chromatographic peak from which the peptide was sequenced; the ≤5 kDa parent fraction reduced intracellular ROS in cultured cells and cell death in zebrafish embryos [65]	Cell-free
Nile tilapia (*Oreochromis niloticus*) skin (f); freshwater comparator, excluded from all counts	KAPDPGPGPM, purified	966.1	DPPH IC_{50} 2.56 mg/mL; binding to Keap1 evaluated by molecular docking [49]	Cell-free (comparator; not counted)

MW = molecular weight; DPPH = 2,2-diphenyl-1-picrylhydrazyl; ABTS = 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); IC_{50} = half-maximal inhibitory concentration; EC_{50} = half-maximal effective concentration; ORAC = oxygen radical absorbance capacity; H_2O_2 = hydrogen peroxide; Keap1 = Kelch-like ECH-associated protein 1; HepG2 = human hepatocellular carcinoma cell line; Hep3B = human hepatoma cell line; TE = Trolox equivalents; ESR = electron spin resonance; GI = gastrointestinal; SOD = superoxide dismutase; CAT = catalase; GSH-Px = glutathione peroxidase; HUVEC = human umbilical vein endothelial cell; PUFA = polyunsaturated fatty acid; ROS = reactive oxygen species. Molecular weights are the values given in the cited studies; entries marked "as reported" differ by more than 1% from the mass calculated from the stated sequence, and where the source reports no mass, the calculated value is given and identified as such. Keys to departures from the scope criteria defined in Section 2.1: (a) the thornback ray entry is an unfractionated hydrolysate for which no sequence was resolved; (d) for the Alaska pollock entry the quoted potency belongs to the purified fraction and not to any single resolved sequence; (f) Nile tilapia is a freshwater species, as described in the primary report [49]; the entry is therefore placed at the foot of the table as a comparator and excluded from every count reported in this review. For the salmon entry the ORAC value is that of the synthesized peptide, whereas the DPPH and hydroxyl radical scavenging, the plasmid DNA protection and the HUVEC result are those of the parent fraction F5; the entry is therefore assigned to the cell-free level. For the seahorse entry the IC_{50} is that of the purified chromatographic peak from which AGD was sequenced, and the cell and zebrafish results belong to the ≤5 kDa parent fraction, so this entry is also assigned to the cell-free level. The seahorse peptide IGTGIPGIW, tested in cultured cells and in zebrafish in the study discussed in Section 5.2, is not tabulated here because that study reports no cell-free measure of antioxidant activity; the most recent report identified for this species that meets all three scope criteria is that on AGD. IC50, EC_{50} and SC_{50} are reproduced as each source study reports them and are not interchangeable, each denoting the concentration producing a 50% effect in the assay named. Of the twenty-three marine entries in Tables 2–4, six were assayed alongside a synthetic antioxidant additive or α-tocopherol: the thornback ray hydrolysate against BHA, HGPLGPL against α-tocopherol and BHT, NHRYDR and GNRGFACRHA against α-tocopherol, and the oyster peptides YAKRCFR and LANAK against BHT.

The hoki entry is the largest such departure in this table, the 797 Da given in the primary report exceeding the 689.8 Da calculated for HGPLGPL by 15.5%; the species in that study is named hoki but identified as *Johnius belengerii*, spelled belangerii in the World Register of Marine Species, whereas hoki technically denotes *Macruronus novaezelandiae*. The skipjack tuna bone collagen peptide SSGPPVPGPMGPMGPR (DPPH IC_{50} 3.15 mM, approximately 4.8 mg/mL) [66] is noted here but not tabulated, because the one-entry-per-species rule retains the more potent and slightly more recent scale gelatin peptide for *Katsuwonus pelamis*. Sequences from thornback ray skin gelatin hydrolysate were resolved in a companion study by the same group, which identified AVGAT as its most active antioxidant peptide at 33% DPPH scavenging at 3 mg/mL [67]; the hydrolysate IC50 it reports is the 1.98 mg/mL given in the primary study [45]. The thornback ray entry is retained at the hydrolysate level because the quoted potency is that of the unfractionated preparation. Units are reproduced as published and are not directly comparable across entries.

Table 3. Representative antioxidant peptides from molluscan sources.

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
Oyster (*Crassostrea rivularis*, currently *Magallana rivularis*)	YAKRCFR, purified	943	DPPH IC50 21.75 µg/mL, with BHT, glutathione and vitamin C as positive controls [50]	Cell culture (Caco-2)
Oyster (*Saccostrea cucullata*) (e)	LANAK, purified	515.29	DPPH scavenging 83.79 ± 0.53%, the highest of the three sequenced peptides, ahead of a 10-mer at 76.62% and a 14-mer at 75.48%; the test concentration is not stated for the purified peptides, the hydrolysate having been assayed over 0.25–1.0 mg/mL, with BHT as positive control [59]	Cell-free
Blue mussel (*Mytilus edulis*), *B. velezensis* protease	VPPFY, synthesized	~622	DPPH scavenging ~60% at 0.1 mg/mL, the highest of five peptides; Keap1 and CD38 binding predicted by docking [40]	Cell-free
Green mussel (*Perna viridis*) (c)	GRTY, sequence resolved within a hydrolysate fraction	638.26 as reported (495.5 calculated)	ABTS IC_{50} 18.3 mg/mL for the whole hydrolysate, not for the isolated peptide; activity attributed to the C-terminal tyrosine [68]	Cell-free
Squid skin collagen (species not specified)	QDGFQGAH, synthesized	900.4 as reported	SC_{50} 0.40 ± 0.05 mg/mL against ABTS, 1.02 ± 0.12 mg/mL against DPPH and 2.77 ± 0.17 mg/mL against hydroxyl radicals; in H_2O_2-challenged HepG2 cells MDA fell by up to 77.7%, Nrf2 rose and Keap1 fell, and SOD, CAT and GSH-Px were elevated; crossed a Caco-2 monolayer intact, P_{app} 4.01 × 10^{-7} cm/s [69]	Cell culture (HepG2)
Abalone (*Haliotis discus hannai*)	DEDEDEDK, synthesized	~994	Most active in cells of ten peptides ranked by Keap1 docking score, though itself lowest-ranked of the ten; raised SOD, CAT and glutathione in AAPH-challenged HUVECs at 250–1000 µg/mL and reduced ROS at 1000 µg/mL; no cell-free assay performed; Keap1-Nrf2 disruption predicted by docking and not verified; carries no aromatic or sulfur-containing residue [42]	Cell culture (HUVEC)

Table 3. *Cont.*

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
Blood cockle (*Tegillarca granosa*)	WPPD, synthesized	513.50	DPPH EC_{50} 0.36 mg/mL; ABTS EC_{50} 0.54 mg/mL; inhibits lipid peroxidation [58]	Cell-free

MW = molecular weight; DPPH = 2,2-diphenyl-1-picrylhydrazyl; ABTS = 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); IC_{50} = half-maximal inhibitory concentration; EC_{50} = half-maximal effective concentration; SC_{50} = concentration giving 50% scavenging; H_2O_2 = hydrogen peroxide; AAPH = 2,2′-azobis(2-amidinopropane) dihydrochloride; MDA = malondialdehyde; ROS = reactive oxygen species; SOD = superoxide dismutase; CAT = catalase; GSH-Px = glutathione peroxidase; Nrf2 = nuclear factor erythroid 2-related factor 2; Keap1 = Kelch-like ECH-associated protein 1; CD38 = cluster of differentiation 38; P_{app} = apparent permeability coefficient; Caco-2 = human colorectal adenocarcinoma cell line; HepG2 = human hepatocellular carcinoma cell line; HUVEC = human umbilical vein endothelial cell. Keys to departures from the scope criteria: (c) for the green mussel entry the quoted potency is that of the whole hydrolysate and not of the resolved sequence; (e) for the oyster (*Saccostrea cucullata*) entry the source states no test concentration for the purified peptides, so the scavenging percentage supports a within-study ranking only. IC_{50}, EC_{50} and SC_{50} are reproduced as each source study reports them and are not interchangeable.

Two earlier *Mytilus edulis* peptides, YPPAK [55] and PIISVYWK [56], are discussed in the text but are not tabulated, because the one-entry-per-species rule retains only the most recent qualifying report. The green mussel entry is a sequence resolved within a characterized hydrolysate fraction rather than a purified peptide: its potency is that of the whole hydrolysate and is not attributable to the sequence alone, and its reported molecular weight of 638.26 Da exceeds the 495.5 Da calculated for GRTY by 28.8%, so the sequence or the mass assignment in the source requires confirmation. Units are reproduced as published and are not directly comparable across entries.

Table 4. Representative antioxidant peptides from crustacean, echinoderm, algal, and cyanobacterial sources.

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
Shrimp shell waste (b)	Crude hydrolysate, <4 kDa	Mixed	DPPH IC_{50} 6.7 mg/mL [60]	Cell-free
Antarctic krill (*Euphausia superba*)	SLPY, purified	~478	DPPH EC_{50} 1.18 mg/mL; stable below 80 °C; activity largely retained through simulated GI digestion [41]	Cell-free
Sea cucumber (*Acaudina molpadioides*) collagen	FLAP, purified	~447	DPPH EC_{50} 0.385 mg/mL [70]; a ≤1 kDa peptide fraction of the same collagen was cytoprotective in macrophages [71]; FLAP itself was active in CCl_4-injured mice [72]	Whole organism (mouse)
Sea cucumber gonad (species not specified)	NPWGQ, synthesized	600.62	DPPH 75.8 ± 0.28% and ABTS 98.9 ± 0.34% scavenging at 5 mg/mL, the highest of four peptides; superoxide dismutase activity raised by 48.1 ± 0.7%; SOD binding predicted by docking and molecular dynamics [73]	Cell-free
Red alga (*Eucheuma cottonii*, currently *Kappaphycus alvarezii*)	YLL, purified	407.51	DPPH EC_{50} 0.52 mM; protected HUVECs from H_2O_2-induced damage [52]	Cell culture (HUVEC)
Red alga (*Gracilariopsis lemaneiformis*)	PGPTY, synthesized	533.57	ABTS IC_{50} 0.24 mg/mL; Keap1 binding predicted by docking; protective in H_2O_2-challenged cells [74]	Cell culture

Table 4. *Cont.*

Source	Peptide or Fraction	MW (Da)	Reported Activity (Ref.)	Highest Validation Level
C-phycocyanin (cyanobacterial protein, *Arthrospira platensis*) (g); inland-water comparator, excluded from all counts	MHLWAAK, synthesized	~856	DPPH IC_{50} 2.593 mg/mL; ABTS IC_{50} 3.362 mg/mL; protective in zebrafish [75]	Whole organism (zebrafish); comparator, not counted

Abbreviations are as defined in the footnotes to Tables 2 and 3; in addition, CCl_4 = carbon tetrachloride and T-SOD = total superoxide dismutase. IC_{50} and EC_{50} are reproduced as each source study reports them and are not interchangeable. Key to departures from the scope criteria: (b) the shrimp shell entry is an unfractionated hydrolysate for which no sequence was resolved. Four of the six peptides isolated in the red algal study were strong radical scavengers and two of those four, YAVT and YLL, protected HUVECs; YLL is tabulated here as the more potent of the two on DPPH, and YAVT is recorded alongside it in Section 5.2. The C-phycocyanin used in the source study was a commercial preparation from *Spirulina platensis* (currently *Arthrospira platensis*), a cyanobacterium cultivated in alkaline inland waters and not obtained from marine environments. This entry is keyed (g), placed at the foot of the table and retained for comparison only; it is excluded from every count reported in this review, meaning that the whole-organism evidence within Tables 2–4 reduces to the single sea cucumber entry. Units are reproduced as published and are not directly comparable across entries.

5. Mechanisms of Action and Levels of Validation

5.1. Direct and Indirect Mechanisms

The compositional patterns described above are consistent with two direct mechanisms by which marine peptides neutralize oxidative damage. Two further routes have been proposed: one acting on antioxidant enzyme activity directly, the other acting indirectly through gene expression.

The first direct mechanism is radical neutralization. In hydrogen atom transfer, aromatic residues, chiefly tyrosine and tryptophan, transfer a hydrogen atom to a radical and form a peptide-derived radical stabilized by delocalization over the ring, whereas sulfur-containing residues donate the hydrogen of a thiol or are oxidized at the thioether sulfur, quenching the radical through a thiyl or sulfoxide product that is not resonance-stabilized; in single electron transfer, the same residues donate an electron directly. Thiyl radicals are not invariably chain-terminating, since they can abstract hydrogen from polyunsaturated fatty acids, so the net effect of a thiol-bearing peptide depends on the system in which it is assayed. The two are grouped here because DPPH and ABTS assays typically capture a mixture of both. The second direct mechanism is metal chelation, which depends on residues capable of coordinating transition metal ions, most commonly the imidazole ring of histidine and the carboxylate side chains of aspartate and glutamate [18,53]. Chelation sequesters catalytic iron and copper and interrupts the Fenton reaction that would otherwise generate hydroxyl radicals. No entry in the sequence-level tables reports a chelation measurement, however, so for the peptides tabulated here this mechanism is inferred from residue composition and has not been directly observed. Accordingly, metal chelation is not attributed to any individual peptide in Tables 2–4.

Inhibition of lipid peroxidation is not a third chemical pathway but a downstream consequence of the two described above. Lipid peroxidation proceeds through initiation, propagation, and termination as radicals abstract hydrogen from polyunsaturated fatty acids and generate lipid radicals that sustain the chain [3]; by scavenging initiating radicals and chelating the metals that catalyze them, a peptide interrupts this cycle. Because many of the peptides listed above act through more than one mechanism concurrently, a single IC_{50} value rarely reflects a peptide's full antioxidant profile, a limitation reflected in machine learning analyses, which score candidates separately for radical-scavenging and metal-

chelation potential [29,76]. A further route has been reported: four peptides from sea cucumber gonad protein raised the measured activity of superoxide dismutase, the most active of them, NPWGQ, by 48.1%, an effect attributed by docking and molecular dynamics to direct binding of the peptides to the enzyme rather than to the transcriptional induction described below [73]. This rests on a single study and on predicted, not measured, binding, so it should be regarded as provisional; NPWGQ is tabulated in Table 4 as the only entry representing this route.

The indirect route, prominent in the more recent literature, operates through gene expression. Under basal conditions, Keap1 binds the transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) and targets it for ubiquitin-mediated degradation; peptides occupying the Kelch domain of Keap1 competitively release Nrf2, which translocates to the nucleus and drives transcription of endogenous antioxidant enzymes through the antioxidant response element [42]. QDGFQGAH and SGDNLRFP from squid skin increased Nrf2 and decreased Keap1 expression in HepG2 cells while elevating superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) [69]; that study and the mackerel work cited above come from one laboratory and dock against the same Keap1 structure, so they are not independent lines of evidence. AP3 (AAAFEGKW), identified in fermented sea cucumber (*Stichopus japonicus*, currently *Apostichopus japonicus*) intestine and assayed as the synthetic peptide, protected HepG2 cells by the same route [77]. Sea cucumber fermented viscera hydrolysate similarly protected Caco-2 cells through the Nrf2/heme oxygenase-1 (HO-1) axis [78]. The mackerel peptides QCCCFT, GNYLLLPPCR, and LHSSSPDFMTR were predicted by docking to bind the Keap1 pocket stably, a result awaiting experimental confirmation, although QCCCFT itself protected hydrogen-peroxide-challenged HepG2 cells in the same study [39]. This mechanism is not detected by cell-free assays: A peptide may be a weak direct scavenger in solution and still increase the total antioxidant capacity of a cell by upregulating the enzymes that mediate scavenging. Three grades of evidence for this route occur among the entries tabulated here, and the validation tables in Section 5.2 are worded so as to distinguish them. An inhibitor experiment, as for the blue mussel peptide whose cytoprotection was abolished by an HO-1 inhibitor [56], supports a functional role for the named enzyme in the observed effect. A change in Nrf2 and Keap1 levels accompanied by elevated enzyme activities, as for QDGFQGAH [69], shows that the pathway responds but does not establish that the peptide binds Keap1. A docking result alone, as for DEDEDEDK [42], predicts an interaction that the cell experiments reported alongside it did not test. None of the three amounts to a measured peptide–Keap1 binding affinity, which no study tabulated here reports.

5.2. Levels of Validation, from Cell-Free Assay to Living Organism

Antioxidant claims for marine peptides are established through a graded hierarchy of evidence, and the validation column recorded in each sequence-level table indicates how unevenly that hierarchy is represented. Three levels are used, and each row is assigned to exactly one of them, namely the highest level reached for the tabulated entry itself. Cell-free denotes that the claim rests on chemical assays in solution, with or without a computational prediction; cell culture denotes that the tabulated entry was applied to cultured cells and produced a measured cellular outcome, whether preserved viability, a change in an oxidative marker such as ROS or malondialdehyde, or a change in the expression or activity of an endogenous antioxidant system; whole organism denotes that the entry was administered to an intact animal. Where the cellular data reported in a study belong to the fraction from which a sequence was resolved rather than to the sequence itself, as for the salmon and seahorse entries, the row is assigned to the cell-free level and the fraction-level result is identified in the table. Of the twenty-three marine entries in Tables 2–4,

which comprise twenty single sequences together with two hydrolysates and one fraction, fourteen reach no further than a cell-free assay at the level of the tabulated entry, eight extend to cultured cells, and one to a whole organism; the two comparator entries, keyed (f) and (g), are excluded from these counts. Cell-free chemical assays such as DPPH, ABTS, and ORAC measure radical-scavenging capacity in solution but provide no information on whether a peptide survives digestion, crosses a cell membrane, or functions within a living system. At the second level, a purified peptide is tested for protection of cultured cells against induced oxidative damage; the most informative such report concerns the blue mussel peptide PIISVYWK, whose protection of cultured hepatocytes was abolished by the heme oxygenase-1 inhibitor zinc protoporphyrin, supporting a role for that enzyme in the protective effect [56]. The peptide tested was synthesized from the sequence identified in the same study; its identity is discussed in Section 4. More recent work has extended this level to squid skin and sea cucumber peptides acting through Keap1-Nrf2 or Nrf2/HO-1 rather than by scavenging alone [69,77,78]. Table 5 sets each tabulated entry against the readouts reported for it and shows which readouts are absent across the set. Representative reports at these first two levels are summarized in Table 6.

Fewer studies extend to the third level, that of whole-animal models; the reports available are consistent in direction but limited in number. Fish collagen peptides from great hammerhead shark (*Sphyrna mokarran*) skin, given orally to ulcer-induced rats, restored endogenous antioxidant enzyme activity and reduced gastric lipid peroxidation [79]. Two further reports merit closer examination. Collagen peptides from *Harpadon nehereus* bone, given to streptozotocin-diabetic mice at 240 mg/kg, reduced blood glucose by 32.8% and improved markers of oxidative stress and glucose metabolism, linking antioxidant activity to a disease outcome instead of an assay endpoint [80]. In the green-lipped mussel *Perna canaliculus*, an Alcalase-derived protein fraction raised catalase and glutathione in the liver and heart of toxin-challenged mice, but in the kidney that effect belonged to the lipid fraction assayed in parallel, which also accounted for most of the reduction in lipid peroxidation, so the outcome cannot be attributed to peptides alone [81]. Elsewhere, a ≤1 kDa peptide fraction of sea cucumber collagen protected macrophages [71], and the tetrapeptide FLAP from the same collagen protected carbon tetrachloride-injured mice [72], phycobiliprotein-derived peptides suppressed ROS in zebrafish embryos without observable toxicity [75], crimson snapper scale peptides prolonged survival in *Drosophila melanogaster* [82], and the seahorse (*H. abdominalis*) peptide IGTGIPGIW was active in cell and zebrafish photoaging models [83]. Human evidence remains preliminary and does not yet point in the expected direction. The only controlled study, a single-blind trial of marine collagen peptides given with plant antioxidants, improved skin parameters but left glutathione, coenzyme Q10, glutathione peroxidase, and glutathione S-transferase unchanged, while plasma superoxide dismutase 3 activity fell and malondialdehyde rose, both within normal ranges [84]; a 90-day single-arm observational study of a multi-component fish collagen preparation reported no significant change in mean serum superoxide dismutase, from 192.13 to 188.43 U/mL ($p = 0.263$), the 31% figure given in its abstract being the proportion of participants whose values rose rather than the magnitude of any rise [85]; a meta-analysis in an adjacent indication found the pooled benefit of collagen supplements no longer apparent once restricted to high-quality and non-industry-funded trials [86]. A broader review reports higher endogenous antioxidant enzyme expression and reduced lipid peroxidation across rodent and zebrafish studies [87]. Whole-organism and human reports are summarized in Table 7.

Two caveats qualify these findings. First, in vivo confirmation is far less common than in vitro reporting, and much of the animal work employs whole hydrolysates or collagen-peptide mixtures rather than the purified sequences listed in the sequence-level tables. Seven of the nine entries in Table 7 are animal studies and two are human studies. Three

concern defined sequences, one of those being the non-marine comparator material, and six concern hydrolysates, collagen-peptide preparations, or multi-component formulations; in the green-lipped mussel study some of the effects were associated with the lipid fraction assayed in parallel, one human study administered collagen peptides together with plant antioxidants, and the other administered them with bovine colostrum powder, coenzyme Q10, calcium and vitamin D3 in an uncontrolled single-arm design. No effect reported in those six can be attributed to an individual sequence, so the whole-organism and human evidence summarized here supports the preparations tested and not the peptides tabulated in Tables 2–4. Second, cell-free or cell-culture potency does not guarantee that a peptide survives gastrointestinal digestion, crosses the intestinal barrier, and reaches target tissue at an active concentration; a review of antioxidant peptides from edible aquatic animals reports that few withstand digestion intact [18]. The concentrations at which the second-level entries in Table 6 were tested range from about 1 µM to more than 1 mM, and no plasma or tissue concentration has been measured for any of them after administration; even hydroxyproline-containing di- and tripeptides, which reach comparatively high plasma concentrations after oral intake of gelatin hydrolysate, peak at about 0.7 to 61 µM in humans [88]. Attainment of the effective concentrations in vivo has therefore not been established for any entry, and the cell-culture level indicates cellular capacity rather than efficacy in vivo. Digestion is not uniformly destructive, however: the activity of Alaska pollock skin collagen hydrolysate rose across two rounds of simulated digestion [64], and a purified krill peptide retained most of its radical-scavenging activity after 180 min and was stable below 80 °C [41]. Digestive stability is therefore attainable, but neither guaranteed nor routinely demonstrated.

Survival of digestion is necessary but not sufficient, since an intact peptide must also traverse the intestinal epithelium. Food-derived peptides are absorbed primarily through the proton-coupled oligopeptide transporter PepT1, whose substrates are di- and tripeptides, and through the slower, less selective paracellular route [89]. Most marine antioxidant peptides characterized to date exceed three residues and are therefore unlikely to be efficient PepT1 substrates, leaving the paracellular route and transcytosis as the plausible pathways. Direct evidence is scarce but not absent: the squid skin octapeptide QDGFQGAH crossed a Caco-2 monolayer intact with an apparent permeability of 4.01×10^{-7} cm/s, of the same order as values reported for other food-derived peptides [69]. Whether transfer at that rate is sufficient to deliver an active concentration to tissue has not been established [90], and QDGFQGAH is the only peptide in the tables above for which transport was measured at all.

Table 5. Readouts reported for each entry in Tables 2–4.

Entry (Peptide or Fraction, Source)	Cell-Free Radical Assay	Metal Chelation Assay	Cell Culture	Whole Organism	Named Reference Antioxidant
TRGH-A26 hydrolysate (thornback ray)	Yes	—	—	—	Yes (BHA)
PMRGGGGYHY (salmon skin collagen)	Yes	—	Fraction only	—	Yes (vitamin C, fraction)
FPYLRH (miiuy croaker)	Yes	—	Yes	—	Yes (ascorbic acid)
HGPLGPL (hoki skin gelatin)	Yes	—	Yes	—	Yes (α-tocopherol, BHT)
DGPKGH (skipjack tuna scale gelatin)	Yes	—	—	—	Yes (glutathione)

Table 5. *Cont.*

Entry (Peptide or Fraction, Source)	Cell-Free Radical Assay	Metal Chelation Assay	Cell Culture	Whole Organism	Named Reference Antioxidant
Fraction A1a3c-p (Alaska pollock)	Yes	—	—	—	—
QCCCFT (mackerel)	Yes	—	Yes	—	—
NHRYDR (horse mackerel)	Yes	—	—	—	Yes (α-tocopherol)
GNRGFACRHA (croaker)	Yes	—	—	—	Yes (α-tocopherol)
AGD (big-belly seahorse)	Yes	—	Fraction only	Fraction only	—
YAKRCFR (oyster *C. rivularis*)	Yes	—	Yes	—	Yes (BHT)
LANAK (oyster *S. cucullata*)	Yes	—	—	—	Yes (BHT)
VPPFY (blue mussel)	Yes	—	—	—	Yes (glutathione, vitamin C)
GRTY (green mussel)	Yes	—	—	—	—
QDGFQGAH (squid skin)	Yes	—	Yes	—	—
DEDEDEDK (abalone)	—	—	Yes	—	—
WPPD (blood cockle)	Yes	—	—	—	—
Crude hydrolysate < 4 kDa (shrimp shell)	Yes	—	—	—	—
SLPY (Antarctic krill)	Yes	—	—	—	Yes (glutathione)
FLAP (sea cucumber collagen)	Yes	—	Fraction only	Yes	—
NPWGQ (sea cucumber gonad)	Yes	—	—	—	—
YLL (red alga *E. cottonii*)	Yes	—	Yes	—	—
PGPTY (red alga *G. lemaneiformis*)	Yes	—	Yes	—	—
KAPDPGPGPM (Nile tilapia) (f), comparator	Yes	—	—	—	—
MHLWAAK (C-phycocyanin) (g), comparator	Yes	—	—	Yes	—

Yes indicates that the readout was reported for the tabulated entry itself. Fraction only indicates that the cell-culture or whole-organism result belongs to a peptide fraction and not to the tabulated sequence, so it does not determine the level assigned in Tables 2–4: the salmon and seahorse entries are therefore assigned to the cell-free level, and the sea cucumber collagen entry reaches the whole-organism level through its own animal data. The final two rows are the comparator entries keyed (f) and (g) in Tables 2 and 4, which are excluded from every count reported in this review. Of the twenty-three marine entries, twenty-two were assayed in at least one cell-free radical assay, none in a metal-chelation assay, eight in cultured cells, one in a whole organism, and eleven alongside a named reference antioxidant, six of those against a synthetic antioxidant additive or α-tocopherol. Because the metal-chelation column is empty, the chelation mechanism described in Section 5.1 rests on residue composition alone. For the green mussel entry the cell-free value is that of the whole hydrolysate, as keyed (c) in Table 3.

Table 6. Validation of marine antioxidant peptides in cell-free and cell-culture models.

Peptide or Preparation (Source)	Reported Effect or Proposed Mechanism	Model	Concentration Tested in Cells (Approx. Molar); Attainment In Vivo	Result	Ref.
SLPY (Antarctic krill)	Radical neutralization	DPPH, hydroxyl, superoxide assays; simulated digestion	Not applicable (cell-free only)	Activity largely retained after 180 min simulated digestion; stable below 80 °C	[41]
TRGH-A26 hydrolysate (thornback ray)	Radical neutralization	DPPH, β-carotene bleaching	Not applicable (cell-free only)	DPPH IC_{50} 1.98 ± 0.02 mg/mL; β-carotene bleaching inhibited by 73.02 ± 1.90%; no cell or animal data reported	[45]
WPPD, MDLFTE (blood cockle)	Radical neutralization	DPPH, hydroxyl, superoxide, ABTS; lipid peroxidation	Not applicable (cell-free only)	EC_{50} 0.36–0.96 mg/mL; lipid peroxidation inhibited	[58]
YAKRCFR (oyster)	Radical neutralization	Caco-2 cells, H_2O_2 challenge	0.1–100 mg/mL; protective at 0.5–10 mg/mL (≈530–10,600 µM); not established	Protected cells from oxidative damage; viability was the only cellular readout reported	[50]
FPYLRH (miiuy croaker *Miichthys miiuy* swim bladder)	Radical neutralization; endogenous enzyme activities raised	HUVECs, H_2O_2 challenge	100 µM; not established	Viability restored to 80.6% at 100 µM; SOD and GSH-Px raised; ROS, MDA and nitric oxide reduced	[62]
HGPLGPL (hoki skin gelatin)	Radical neutralization; endogenous enzyme activities raised	Hep3B cells	150 µg/mL (≈190 µM); not established	SOD, GSH-Px and CAT activities elevated	[63]
PIISVYWK (blue mussel)	Radical neutralization; role of HO-1 supported by inhibitor experiment	Hepatocytes, H_2O_2 challenge	100–300 µM; not established	Increased viability; HO-1 upregulated; protection abolished by an HO-1 inhibitor	[56]
YAVT, YLL (EP4, EP5; red alga *E. cottonii*)	Radical neutralization	HUVECs, H_2O_2 challenge	100–200 µM; not established	Protected cells and inhibited progression to late apoptosis; elevated antioxidant enzyme levels	[52]
PGPTY (red alga *G. lemaneiformis*)	Radical neutralization; Keap1 binding predicted by docking, not measured	ABTS assay, docking, H_2O_2-challenged cells	100 µg/mL (≈190 µM); not established	ABTS IC_{50} 0.24 mg/mL; cell viability preserved	[74]
LKPGN, LQP (Antarctic krill)	Radical neutralization	Chang liver cells, H_2O_2 challenge	100–400 µM; not established	Viability increased and apoptosis reduced concentration-dependently; antioxidant enzyme activity raised, DNA damage and MDA lowered	[91]

Table 6. *Cont.*

Peptide or Preparation (Source)	Reported Effect or Proposed Mechanism	Model	Concentration Tested in Cells (Approx. Molar); Attainment In Vivo	Result	Ref.
QCCCFT (mackerel *Pneumatophorus japonicus*, currently *Scomber japonicus*)	Radical neutralization; Keap1 binding predicted by docking, not measured	DPPH, ABTS, hydroxyl assays; molecular dynamics; HepG2 cells, H_2O_2 challenge	1–20 µg/mL (≈1.4–28 µM); not established	Most active of 14 synthesized sequences; MDA and LDH release reduced, SOD and CAT raised, apoptosis attenuated	[39]
QDGFQGAH (squid skin)	Nrf2 raised and Keap1 lowered with enzyme activities elevated; Keap1-Nrf2 involvement proposed, binding not measured	H_2O_2-challenged cells	0.0625–1 mg/mL (≈69–1110 µM); not established	Nrf2 increased and Keap1 decreased; SOD, CAT and GSH-Px elevated; MDA reduced by up to 77.7%	[69]
DEDEDEDK (abalone)	Enzyme activities raised and ROS lowered in cells; Keap1 binding predicted by docking and not tested	HUVECs, AAPH challenge	250–1000 µg/mL (≈250–1000 µM); not established	SOD, CAT and glutathione raised at 250–1000 µg/mL; ROS reduced at 1000 µg/mL; Keap1 binding predicted by docking, not verified	[42]
AP3, AAAFEGKW (fermented sea cucumber intestine)	Radical scavenging; Nrf2 pathway activation proposed	HepG2 cells, oxidative challenge	5–50 µM; not established	At 1000 µMol/L the synthetic peptide scavenged DPPH 53.0%, superoxide 65.1% and hydroxyl radicals 54.2%; in cells ROS and MDA reduced and endogenous enzyme activities elevated	[77]
Fermented viscera hydrolysate (sea cucumber)	Nrf2/HO-1 activation proposed	Caco-2 cells, oxidative challenge	0.016–0.4 mg/mL (hydrolysate; no molar value); not established	Antioxidant capacity enhanced; cell metabolism improved	[78]

MDA = malondialdehyde; ROS = reactive oxygen species; LDH = lactate dehydrogenase; DPPH = 2,2-diphenyl-1-picrylhydrazyl; ABTS = 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); IC_{50} = half-maximal inhibitory concentration; EC_{50} = half-maximal effective concentration; H_2O_2 = hydrogen peroxide; SOD = superoxide dismutase; CAT = catalase; GSH-Px = glutathione peroxidase; Nrf2 = nuclear factor erythroid 2-related factor 2; Keap1 = Kelch-like ECH-associated protein 1; HO-1 = heme oxygenase-1; HUVEC = human umbilical vein endothelial cell; HepG2 = human hepatocellular carcinoma cell line; Hep3B = human hepatoma cell line; Caco-2 = human colorectal adenocarcinoma cell line. EP4 and EP5 are the source study's designations for the two red algal peptides. Other abbreviations are as defined above. The second column separates effects that were measured from mechanisms that were proposed: an effect is stated without qualification only where the cited study measured it directly, whereas an interaction identified by molecular docking is stated as predicted. No study listed here reports a measured peptide–Keap1 binding affinity. Approximate molar concentrations are calculated from the molecular masses given in Tables 2–4 or from the sequence. No study listed here measured the plasma or tissue concentration of the peptide after administration, so attainment in vivo of the concentrations tested has not been established for any entry; for comparison, hydroxyproline-containing di- and tripeptides, which reach comparatively high plasma concentrations after oral intake of gelatin hydrolysate, peak at about 0.7 to 61 µM in humans [88], a range within which only QCCCFT and AP3 were tested.

Table 7. Validation of marine antioxidant peptides in whole-organism and human studies.

Peptide or Preparation (Source)	Reported Effect or Proposed Mechanism	Model	Result	Ref.
Collagen peptides (great hammerhead shark *S. mokarran* skin)	Endogenous enzyme activities restored	Ulcer-induced rats, oral	Ulcerative lesions inhibited by 86%; gastric SOD and CAT activities restored; lipid peroxidation reduced	[79]
Collagen peptides (*H. nehereus* bone)	Redox and glucose regulation	Streptozotocin-diabetic mice, 240 mg/kg oral	Blood glucose reduced 32.8%, triglyceride 42.2%; hepatic Nrf2 up-regulated and oxidative markers improved	[80]
Protein and lipid fractions (green-lipped mussel *P. canaliculus*)	Endogenous enzyme activities raised	Toxin-challenged mice, oral	Protein fraction raised CAT and glutathione in liver and heart; in the kidney the lipid fraction did so, and it also accounted for most of the reduction in lipid peroxidation	[81]
FLAP, defined synthesized sequence (sea cucumber *Acaudina molpadioides* collagen)	Nrf2 and HO-1 upregulated; pathway involvement proposed	CCl_4-induced liver and kidney injury, mice	CAT, SOD and GSH-Px activities raised; Nrf2 and HO-1 upregulated; inflammatory markers reduced	[72]
MHLWAAK, MAQAAEYYR, MDYYFEER, defined synthesized sequences (C-phycocyanin; non-marine comparator)	Nrf2 pathway upregulation proposed	Zebrafish embryos, H_2O_2	ROS and MDA reduced; no observed toxicity	[75]
Scale peptides (crimson snapper)	Endogenous enzyme activities raised	*Drosophila melanogaster*, oxidative challenge	Mean and maximum lifespan extended and motor ability improved; MDA and protein carbonyl lowered, T-SOD, CAT and GSH-Px raised; mTOR signaling downregulated and autophagy activated at 6 mg/mL	[82]
IGTGIPGIW (SHP2), defined sequence purified from hydrolysate (seahorse, *Hippocampus abdominalis*)	Redox modulation	UVB-irradiated HaCaT and HDF cells; UVB-irradiated zebrafish	ROS and lipid peroxidation suppressed, collagen synthesis improved and MMP secretion reduced in cells; cell death and ROS reduced in zebrafish at 200 µg/mL	[83]
Marine collagen peptides with plant antioxidants	Systemic redox modulation	Human, single-blind case-control	Plasma SOD3 activity fell and MDA and nitrite/nitrate rose, all within normal ranges; GSH, coenzyme Q10, GSH-Px and GST unchanged	[84]
Fish collagen peptides with bovine colostrum powder, coenzyme Q10, calcium and vitamin D3	Systemic redox modulation	Human, 90 days, single-arm observational	Mean SOD unchanged over 90 days in 29 women, 192.13 to 188.43 U/mL ($p = 0.263$); the 31.03% given in the abstract is the share of subjects with elevated values, 9 of 29; uncontrolled single-arm design	[85]

Abbreviations are as defined above; GSH = glutathione; GST = glutathione S-transferase; SOD3 = superoxide dismutase 3; T-SOD = total superoxide dismutase; MMP = matrix metalloproteinase; UVB = ultraviolet B; CCl_4 = carbon tetrachloride; HaCaT = human keratinocyte line; HDF = human dermal fibroblast; mTOR = mechanistic target of rapamycin. Several entries are hydrolysates or peptide complexes for which no single sequence was resolved, and the green-lipped mussel entry is a comparison of protein, lipid, and polysaccharide fractions in which non-peptide material contributed to the effect; these fall outside the sequence-level scope criteria applied to the earlier tables and are included because whole-organism evidence is otherwise sparse. The second column separates measured effects from proposed mechanisms, by the same convention as Table 6. Seven of the nine entries are animal studies and two are human studies. Three concern defined sequences, namely FLAP, the seahorse peptide IGTGIPGIW and the three C-phycocyanin peptides, and six concern hydrolysates, collagen-peptide preparations, or multi-component formulations; no biological effect reported for the latter six can be attributed to an individual sequence. The C-phycocyanin entry derives from *Arthrospira platensis*, a cyanobacterium cultivated in inland waters, and is the comparator keyed (g) in Table 4.

6. Translational Outlook and Limitations

6.1. Commercial Context

Commercial interest is evident, but its scale cannot be established from the available sources: the only estimates are two proprietary, non-peer-reviewed market analyses that differ by nearly an order of magnitude and agree only on the direction of growth [92,93]. A peer-reviewed assessment identifies the principal constraints as scalability of isolation, regulatory approval pathways, and consumer acceptance; demand is not among them [94].

6.2. Safety and Matrix-Derived Risks

Two hazards derive from the feedstock rather than from the peptides themselves, and neither is routinely reported alongside potency. The first is allergenicity. Parvalbumin in fish and tropomyosin in invertebrates are the dominant seafood allergens, and both are heat-stable; the evidence bearing directly on enzymatic hydrolysis, however, concerns tropomyosin. Pepsin digestion of fish tropomyosin progressively lowers the antigenicity of the intact protein, on which two immunoglobulin E-binding epitopes have been identified [95]. Maillard glycation of molluscan tropomyosin modifies most of its defined epitopes and reduces its immunoreactivity [96]. Whether parvalbumin epitopes behave comparably under the hydrolysis conditions used to generate antioxidant peptides has not been established. Enzymatic hydrolysis reduces antigenicity but does not necessarily abolish it; therefore, a hydrolysate marketed as an antioxidant ingredient remains subject to the allergen-labeling requirements of its source species; a purified single peptide is less exposed to this concern than the hydrolysates and peptide complexes that dominate the whole-organism literature. The second is elemental contamination. In a decade of Italian official-control monitoring covering 2014 to 2023, cadmium above the regulatory limit was recorded in 22 of the 3338 samples analyzed for it, or 0.7%, 17 of them cephalopod molluscs, mainly squid, at 1.40 to 5.60 mg/kg [97], and heavy metals bind C-phycocyanin isolated from wild freshwater cyanobacterial biomass [98]. Both matrices are represented among the peptides tabulated above. Neither hazard bears on the antioxidant claims themselves, but both must be addressed before pharmaceutical or nutraceutical use. Disclosure of the source material and of the contaminant levels measured in it is the minimum requirement and is not itself a safety assessment: the allergenicity of the parent protein remaining after purification, the contaminant burden of the finished preparation rather than of the raw material, and tolerance at the doses proposed for administration each require dedicated characterization, which, as noted in the Introduction, has not been reported for the peptides reviewed here. Both hazards also depend on the degree of purification: A purified short peptide is less likely to retain intact epitopes of the parent allergen or the elemental burden of the feedstock, whereas the hydrolysates and peptide complexes that dominate the whole-organism and human literature may retain both.

6.3. Performance Relative to Established Synthetic Antioxidants

Direct comparison with the compounds these peptides are proposed to replace is more frequent than reported potency values alone suggest, but it is confined to chemical systems. Six of the twenty-three tabulated marine entries were assayed alongside a synthetic antioxidant additive or α-tocopherol: the thornback ray hydrolysate against BHA [45]; the oyster peptides YAKRCFR and LANAK against BHT [50,59]; the hoki skin gelatin peptide HGPLGPL, which inhibited linoleic acid peroxidation more than α-tocopherol did and almost as well as BHT [63]; and the horse mackerel and croaker peptides NHRYDR and GNRGFACRHA, both of which inhibited polyunsaturated fatty acid peroxidation more effectively than α-tocopherol [54]. Five further entries were assayed against a reference antioxidant that is not a candidate replacement, namely ascorbic acid, vitamin C or glu-

tathione [40,41,46,51,61]. All of these comparisons were made in chemical or model lipid systems; none was made in a food, pharmaceutical, or nutraceutical matrix, and none used TBHQ. In most primary reports the comparator appears in the methods or figures rather than alongside the headline potency value. Antioxidant proteins and peptides have been assessed more broadly as a means of improving the oxidative stability of muscle foods [99], and antioxidant peptides have been evaluated in fish-oil-in-water emulsions and fish-oil-enriched mayonnaise and not merely in buffer [100]. Matrix-level tests of this kind are the most directly relevant evidence for a replacement claim, yet no entry tabulated here was tested in one, and such tests are currently confined almost entirely to food matrices; equivalent formulation-level data for pharmaceutical and nutraceutical preparations were not identified in this search. A sensory constraint may compound this difficulty, as hydrophobic residues, which are commonly found in the most active sequences, are also associated with bitterness in fish protein hydrolysates [101].

6.4. Current Limitations

Five limitations of quality recur throughout this literature. Reporting is not standardized: the incompatible potency units described above preclude ranking without re-analysis of the raw data—percentage scavenging at a single concentration, EC_{50} and IC_{50} on mass and on molar bases, oxygen radical absorbance in Trolox equivalents and the concentration halving an ESR signal all appear among the twenty-three tabulated marine entries—and two of those entries support no more than a within-study ordering, one resting on effects recorded at defined test concentrations and not on a potency value of any kind, the other on a scavenging percentage for which the source states no test concentration. A validation gap persists; since most reported peptides have been tested only in cell-free assays or cultured cells, in vivo work often employs whole hydrolysates in place of the individual sequences whose potency is best characterized, human evidence is limited to small studies of largely uncontrolled design, and the digestive stability and intestinal transport on which any oral effect depends are rarely measured. The computational tools present a distributional problem: predictors are trained largely on general or food-protein datasets rather than marine-specific ones, so their reported accuracies, which reach 0.97 on one standard benchmark but fall to 0.80 on another, describe performance on distributions to which marine sequences may not belong [33]; their predictions are best treated as a prioritization aid. The allergen and elemental risks described above are not reported in the sequence-level studies reviewed here. Finally, there is a limitation related to the assays rather than to the peptides. DPPH and ABTS are synthetic radicals that do not occur in animal tissues, and for DPPH the value returned depends on the solvent and the pH chosen and on the reaction time allowed, since the assay records an endpoint and not a rate; none of these conditions is standardized across the studies tabulated here [102]. Three further sources of error apply unevenly across the entries in Tables 2–4. The first is optical interference: A test material that absorbs at the wavelength read alters the apparent value unless a sample blank is subtracted, which several but not all of the primary reports state; reducing-power assays, moreover, register any electron donation to Fe(III) and so do not distinguish antioxidant activity from reducing capacity in general. The second is pro-oxidant behavior, since the histidine and cysteine residues credited with metal binding are themselves redox-active and may return a bound metal to catalysis; hydroxyl radical scavenging measured in Fenton-type systems, reported for many of the entries, indicates a net antioxidant outcome under those conditions, but no study tested the peptides under conditions designed to reveal pro-oxidant activity, and the Fenton-interruption argument of Section 5.1 therefore remains an inference from composition. The third is the absence of in-batch calibration: A named reference antioxidant assayed in the same batch is reported for eleven of the twenty-three entries, meaning that for the

remaining twelve the contribution of inter-laboratory variation cannot be separated from the difference between peptides. Of these four assay-related limitations, the dependence on assay conditions is documented in each report and therefore restricts comparison between studies rather than within them; optical interference can be set aside only where a sample blank was reported; pro-oxidant behavior cannot be excluded for any entry, although the Fenton-type data argue against it under the conditions tested; and the absence of in-batch calibration cannot be remedied for the twelve entries concerned.

6.5. Research Priorities

A priority follows from each of these. Methodologically, adoption of a minimum reporting set, comprising assay identity, peptide purity, concentration on a defined mass or molar basis and a common reference standard such as Trolox equivalents, would address the comparability problem at its source without new experimental work. On delivery, encapsulation addresses the bioavailability problem embedded in the validation gap: liposomes, polymer nanoparticles and related carriers have improved the stability and retained the bioactivity of bioactive peptides generally [103], have increased in vivo efficacy for chitosan-encapsulated antihypertensive biopeptides of marine origin [104], and are now being formulated specifically for marine peptide systems [105]. Computationally, coupling marine-specific predictive models to targeted experimental validation would accelerate progression from raw by-product to characterized ingredient. On safety, disclosure of the source material and of measured contaminant levels alongside potency is an immediate and inexpensive step, but it does not substitute for toxicological characterization of the finished preparation, including residual allergenicity after purification and tolerance at the intended dose. The priority on which the others depend is adequately powered, placebo-controlled human evaluation establishing that in vitro potency translates into measurable clinical benefit [87].

7. Conclusions

Marine antioxidant peptides are obtained primarily by enzymatic hydrolysis of proteins from fish, molluscs, crustaceans, echinoderms, algae and cyanobacteria, much of which is recovered from processing by-products; machine learning tools now supplement, rather than replace, this workflow. Aromatic and sulfur-containing residues, residue position and, less consistently, hydrophobicity recur among the most potent peptides, though not as requirements: three of the twenty tabulated marine sequences carry neither an aromatic nor a sulfur-containing residue. Chain length shows no consistent relationship with potency across this set, which comprises the most active sequences of each retained study and is therefore not a representative sample of marine antioxidant peptides. These features support radical neutralization by hydrogen atom or single electron transfer and transition metal chelation, alongside an indirect route through Keap1-Nrf2 that cell-free assays do not detect and that has been proposed to account for one of those three sequences. For defined sequences, supporting evidence weakens progressively from cell-free assays to cultured cells and whole organisms: of the twenty-three tabulated marine entries, fourteen reach only a cell-free assay, eight cultured cells and one a whole organism, and none of the concentrations tested in cells has been shown to be attainable in vivo. The nine animal and human studies tabulated in parallel concern mostly hydrolysates or multi-component preparations rather than defined sequences, so they support those preparations and not individual peptides. Human data remain preliminary, and a synthetic antioxidant or α-tocopherol was used as comparator for six of the twenty-three entries, in every case in a chemical or model lipid system and never in a food matrix. Marine antioxidant peptides therefore constitute credible but not yet substantiated candidates, both as replacements for synthetic antioxidant additives and as bioactive ingredients. Four further gaps must be

addressed before this potential can be confirmed: potency is reported in units that cannot be compared across studies and is obtained in assays that are neither standardized nor calibrated against a common reference; predictive models are trained on distributions to which marine sequences may not belong; allergen and heavy-metal risks are not reported alongside potency; and toxicological characterization of finished preparations has not been reported for the peptides reviewed here. Standardized reporting, encapsulation-based delivery, marine-specific predictive models, disclosure of matrix-derived risk together with toxicological characterization of finished preparations, and adequately powered clinical evaluation make up the measures most likely to advance the field from characterization to therapeutic application.

Author Contributions: Y.G.P. and J.-W.J.: Conceptualization, Methodology, Investigation, Data Curation, Writing—Original Draft Preparation. S.-C.K. (Seok-Chun Ko), M.-J.Y., J.-Y.K. and D.Y.: Conceptualization, Methodology, Writing—Original Draft Preparation. S.-H.J., S.-C.K. (Se-Chang Kim) and J.M.L.: Investigation, Data Curation. D.-S.L.: Conceptualization, Methodology. H.-S.K. and G.-W.O.: Supervision, Conceptualization, Methodology, Data Curation, Writing—Original Draft Preparation. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by the National Marine Biodiversity Institute of Korea Research Program 2026M00500.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Acknowledgments: During the preparation of this manuscript, the authors used Claude (Opus 5, Anthropic) to assist with language editing, verification of reported values and bibliographic details against the cited sources, and suggestions for revised wording; all suggestions were checked against the primary literature by the authors. All tables in this article were compiled by the authors from previously published studies, with the original sources cited in the corresponding cells; as such, no third-party copyright permission is required. The authors have reviewed and edited all AI-assisted output and take full responsibility for the content of this publication.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

BHA	Butylated hydroxyanisole
BHT	Butylated hydroxytoluene
TBHQ	Tert-butylhydroquinone
ROS	Reactive oxygen species
DPPH	2,2-diphenyl-1-picrylhydrazyl
ABTS	2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
ORAC	Oxygen radical absorbance capacity
FRAP	Ferric reducing antioxidant power
ESR	Electron spin resonance
TE	Trolox equivalents
IC_{50}	Half-maximal inhibitory concentration
EC_{50}	Half-maximal effective concentration
SC_{50}	Concentration giving 50% scavenging
HPLC	High-performance liquid chromatography
LC-MS/MS	Liquid chromatography–tandem mass spectrometry
ESI-MS	Electrospray ionization mass spectrometry
DFT	Density functional theory
LSTM	Long short-term memory

Bi-LSTM	Bidirectional long short-term memory
SHAP	SHapley Additive exPlanations
Keap1	Kelch-like ECH-associated protein 1
Nrf2	Nuclear factor erythroid 2-related factor 2
HO-1	Heme oxygenase-1
SOD	Superoxide dismutase
SOD3	Superoxide dismutase 3
T-SOD	Total superoxide dismutase
CAT	Catalase
GSH-Px	Glutathione peroxidase
GSH	Glutathione
GST	Glutathione S-transferase
MDA	Malondialdehyde
LDH	Lactate dehydrogenase
GI	Gastrointestinal
PUFA	Polyunsaturated fatty acid
PepT1	Proton-coupled oligopeptide transporter 1
P_{app}	Apparent permeability coefficient
AAPH	2,2′-azobis(2-amidinopropane) dihydrochloride
MMP	Matrix metalloproteinase
UVB	Ultraviolet B
CCl_4	Carbon tetrachloride
mTOR	Mechanistic target of rapamycin
CD38	Cluster of differentiation 38
HUVEC	Human umbilical vein endothelial cell
HepG2	Human hepatocellular carcinoma cell line
Hep3B	Human hepatoma cell line
Caco-2	Human colorectal adenocarcinoma cell line
HaCaT	Human keratinocyte cell line
HDF	Human dermal fibroblast

References

1. Su, L.J.; Zhang, J.H.; Gomez, H.; Murugan, R.; Hong, X.; Xu, D.; Jiang, F.; Peng, Z.Y. Reactive Oxygen Species-Induced Lipid Peroxidation in Apoptosis, Autophagy, and Ferroptosis. *Oxid. Med. Cell. Longev.* **2019**, *2019*, 5080843. [CrossRef] [PubMed]
2. Sies, H. Oxidative Stress: Concept and Some Practical Aspects. *Antioxidants* **2020**, *9*, 852. [CrossRef] [PubMed]
3. Repetto, M.; Semprine, J.; Boveris, A. Lipid Peroxidation: Chemical Mechanism, Biological Implications and Analytical Determination. In *Lipid Peroxidation*; Catala, A., Ed.; InTech: Rijeka, Croatia, 2012; pp. 3–30. [CrossRef] [PubMed]
4. *Code of Federal Regulations*; Title 21. Substances Generally Recognized as Safe: Butylated Hydroxyanisole, 21 CFR 182.3169; Butylated Hydroxytoluene, 21 CFR 182.3173; Food Additives Permitted for Direct Addition to Food for Human Consumption: BHA, 21 CFR 172.110; BHT, 21 CFR 172.115; US Government Publishing Office: Washington, DC, USA, 2026. Available online: https://www.ecfr.gov/current/title-21 (accessed on 15 September 2026).
5. Ren, J.; Li, Z.; Li, X.; Yang, L.; Bu, Z.; Wu, Y.; Li, Y.; Zhang, S.; Meng, X. Exploring the Mechanisms of the Antioxidants BHA, BHT, and TBHQ in Hepatotoxicity, Nephrotoxicity, and Neurotoxicity from the Perspective of Network Toxicology. *Foods* **2025**, *14*, 1095. [CrossRef] [PubMed]
6. US Food and Drug Administration. FDA Update on Post-Market Assessment of Chemicals in the Food Supply. HFP Constituent Update, 19 August 2025. Available online: https://www.fda.gov/food/hfp-constituent-updates/fda-update-post-market-assessment-chemicals-food-supply-0 (accessed on 15 September 2026).
7. US Food and Drug Administration. Butylated Hydroxyanisole (BHA); Request for Information. In *Federal Register*; Docket No. FDA-2026-N-0302; Office of the Federal Register: Washington, DC, USA; National Archives and Records Administration: Washington, DC, USA, 2026; Volume 91, pp. 6227–6229.
8. US Food and Drug Administration. Butylated Hydroxytoluene (BHT); Request for Information. In *Federal Register*; Docket No. FDA-2026-N-2526; Office of the Federal Register: Washington, DC, USA; National Archives and Records Administration: Washington, DC, USA, 2026; Volume 91, pp. 27054–27056.
9. US Food and Drug Administration. Butylated Hydroxytoluene (BHT); Request for Information; Reopening of Comment Period. In *Federal Register*; Docket No. FDA-2026-N-2526; Office of the Federal Register: Washington, DC, USA; National Archives and Records Administration: Washington, DC, USA, 2026; Volume 91, pp. 48127–48128 (30 July 2026; Document 2026-15429).

10. Gutiérrez-Del-Río, I.; López-Ibáñez, S.; Magadán-Corpas, P.; Fernández-Calleja, L.; Pérez-Valero, Á.; Tuñón-Granda, M.; Miguélez, E.M.; Villar, C.J.; Lombó, F. Terpenoids and Polyphenols as Natural Antioxidant Agents in Food Preservation. *Antioxidants* **2021**, *10*, 1264. [CrossRef] [PubMed]
11. Shahidi, F.; Saeid, A. Bioactivity of Marine-Derived Peptides and Proteins: A Review. *Mar. Drugs* **2025**, *23*, 157. [CrossRef] [PubMed]
12. Zhang, R.; Ren, Y.; Ren, T.; Yu, Y.; Li, B.; Zhou, X. Marine-Derived Antioxidants: A Comprehensive Review of Their Therapeutic Potential in Oxidative Stress-Associated Diseases. *Mar. Drugs* **2025**, *23*, 223. [CrossRef] [PubMed]
13. Shekoohi, N.; Carson, B.P.; Fitzgerald, R.J. Antioxidative, Glucose Management, and Muscle Protein Synthesis Properties of Fish Protein Hydrolysates and Peptides. *J. Agric. Food Chem.* **2024**, *72*, 21301–21317. [CrossRef] [PubMed]
14. Okeke, E.S.; Okagu, I.U.; Chukwudozie, K.; Ezike, T.C.; Ezeorba, T.P.C. Marine-Derived Bioactive Proteins and Peptides: A Review of Current Knowledge on Anticancer Potentials, Clinical Trials, and Future Prospects. *Nat. Prod. Commun.* **2024**, *19*, 1–19. [CrossRef]
15. Guryanova, S.V.; Ovchinnikova, T.V. Multifaceted Marine Peptides and Their Therapeutic Potential. *Mar. Drugs* **2025**, *23*, 288. [CrossRef] [PubMed]
16. Sila, A.; Bougatef, A. Antioxidant Peptides from Marine By-Products: Isolation, Identification and Application in Food Systems—A Review. *J. Funct. Foods* **2016**, *21*, 10–26. [CrossRef]
17. Liu, X.; Hu, Q.; Shen, Y.; Wu, Y.; Gao, L.; Xu, X.; Hao, G. Research Progress on Antioxidant Peptides from Fish By-Products: Purification, Identification, and Structure–Activity Relationship. *Metabolites* **2024**, *14*, 561. [CrossRef] [PubMed]
18. Xiang, Z.; Xue, Q.; Gao, P.; Yu, H.; Wu, M.; Zhao, Z.; Li, Y.; Wang, S.; Zhang, J.; Dai, L. Antioxidant Peptides from Edible Aquatic Animals: Preparation Method, Mechanism of Action, and Structure–Activity Relationships. *Food Chem.* **2023**, *404*, 134701. [CrossRef] [PubMed]
19. Tang, C.D.; Cheng, J.H.; Sun, D.W. Structure–Activity Relationships and Activity Enhancement Techniques of Marine Bioactive Peptides (MBPs). *Crit. Rev. Food Sci. Nutr.* **2025**, *65*, 4941–4963. [CrossRef] [PubMed]
20. Ashaolu, T.J.; Pham, B.P.; Molnár, Z.; Varga, L.; Greff, B. The Structure–Activity Relationship of Marine Peptides: A Review. *Int. J. Food Sci. Technol.* **2024**, *59*, 4437–4445. [CrossRef]
21. Cui, Y.; Li, X.; Sun, Y.; Liu, Y.; Zhang, W.; Jiang, Y.; Zhou, Y.; Liu, J.; Gong, B.; Wu, Y.; et al. Separation, Characterization, AI Screening, and Bioactivities of Marine Bioactive Peptides: A Review. *Food Chem.* **2025**, *495*, 146312. [CrossRef] [PubMed]
22. Cadar, E.; Pesterau, A.M.; Prasacu, I.; Ionescu, A.M.; Pascale, C.; Dragan, A.L.; Sirbu, R.; Tomescu, C.L. Marine Antioxidants from Marine Collagen and Collagen Peptides with Nutraceuticals Applications: A Review. *Antioxidants* **2024**, *13*, 919. [CrossRef] [PubMed]
23. Wang, C.H.; Doan, C.T.; Nguyen, V.B.; Nguyen, A.D.; Wang, S.L. Reclamation of Fishery Processing Waste: A Mini-Review. *Molecules* **2019**, *24*, 2234. [CrossRef] [PubMed]
24. Man, J.; Abd El-Aty, A.M.; Wang, Z.; Tan, M. Recent Advances in Sea Cucumber Peptide: Production, Bioactive Properties, and Prospects. *Food Front.* **2023**, *4*, 131–163. [CrossRef]
25. Hopkins, D.T.; Berrué, F.; Khiari, Z.; Hawboldt, K.A. Valorization of Fisheries By-Products via Enzymatic Protein Hydrolysis: A Review of Operating Conditions, Process Design, and Future Trends. *Process Biochem.* **2025**, *149*, 306–320. [CrossRef]
26. Pérez-Flores, J.G.; García-Curiel, L.; Pérez-Escalante, E.; Contreras-López, E.; Rodríguez-Serrano, G.M.; Rivera-Arredondo, M.; Ocampo-Salinas, I.O.; Sánchez-Franco, J.A.; Paz-Samaniego, R.; Guerrero-Solano, J.A. Alcalase for Food-Protein-Derived Bioactive Peptides: Trends, Gaps, and Translational Opportunities. *Macromol.* **2026**, *6*, 16. [CrossRef]
27. Gao, R.; Yu, Q.; Shen, Y.; Chu, Q.; Chen, G.; Fen, S.; Yang, M.; Yuan, L.; McClements, D.J.; Sun, Q. Production, Bioactive Properties, and Potential Applications of Fish Protein Hydrolysates: Developments and Challenges. *Trends Food Sci. Technol.* **2021**, *110*, 687–699. [CrossRef]
28. Choonpicharn, S.; Jaturasitha, S.; Rakariyatham, N.; Suree, N.; Niamsup, H. Antioxidant and Antihypertensive Activity of Gelatin Hydrolysate from Nile Tilapia Skin. *J. Food Sci. Technol.* **2015**, *52*, 3134–3139. [CrossRef] [PubMed]
29. Olsen, T.H.; Yesiltas, B.; Marin, F.I.; Pertseva, M.; García-Moreno, P.J.; Gregersen, S.; Overgaard, M.T.; Jacobsen, C.; Lund, O.; Hansen, E.B.; et al. AnOxPePred: Using Deep Learning for the Prediction of Antioxidative Properties of Peptides. *Sci. Rep.* **2020**, *10*, 21471. [CrossRef] [PubMed]
30. Liu, X.; Guan, F.; Luo, H.; Yao, B.; Tian, J. Artificial Intelligence-Driven Discovery of Bioactive Peptides: Computational Approaches and Future Perspectives. *aBIOTECH* **2026**, *7*, 100014. [CrossRef] [PubMed]
31. Qin, D.; Jiao, L.; Wang, R.; Zhao, Y.; Hao, Y.; Liang, G. Prediction of Antioxidant Peptides Using a Quantitative Structure-Activity Relationship Predictor (AnOxPP) Based on Bidirectional Long Short-Term Memory Neural Network and Interpretable Amino Acid Descriptors. *Comput. Biol. Med.* **2023**, *154*, 106591. [CrossRef] [PubMed]
32. Hassan, M.T.; Tayara, H.; Chong, K.T. iAnOxPep: A Machine Learning Model for the Identification of Anti-oxidative Peptides Using Ensemble Learning. *IEEE Trans. Comput. Biol. Bioinform.* **2025**, *22*, 85–96. [CrossRef] [PubMed]

33. Cai, J.; Lou, X.; Chong, C.F.; Alex, D.; Arrais, J.P.; Wang, Y.; Siu, S.W.I. Multi-AOP: A Lightweight Multi-view Deep Learning Framework for Antioxidant Peptide Discovery. *Bioresour. Bioprocess.* **2026**, *13*, 21. [CrossRef] [PubMed]
34. Song, J.; Liu, K.; Jin, X.; Huang, K.; Fu, S.; Yi, W.; Cai, Y.; Yu, Z.; Mao, F.; Zhang, Y. Machine Learning-Driven Discovery and Evaluation of Antimicrobial Peptides from *Crassostrea gigas* Mucus Proteome. *Mar. Drugs* **2024**, *22*, 385. [CrossRef] [PubMed]
35. Liao, W.; Yan, S.; Cao, X.; Xia, H.; Wang, S.; Sun, G.; Cai, K. A Novel LSTM-Based Machine Learning Model for Predicting the Activity of Food Protein-Derived Antihypertensive Peptides. *Molecules* **2023**, *28*, 4901. [CrossRef] [PubMed]
36. Zhang, M.; Zhou, J.; Wang, X.; Wang, X.; Ge, F. DeepBP: Ensemble Deep Learning Strategy for Bioactive Peptide Prediction. *BMC Bioinform.* **2024**, *25*, 352. [CrossRef] [PubMed]
37. Li, W.; Liu, X.; Liu, Y.; Zheng, Z. High-Accuracy Identification and Structure–Activity Analysis of Antioxidant Peptides via Deep Learning and Quantum Chemistry. *J. Chem. Inf. Model.* **2025**, *65*, 603–612. [CrossRef] [PubMed]
38. Cheng, S.; Chen, Y.; Cao, Y.; Huang, X.; Liu, B.; Liu, M.; Jiang, S.; Jiang, L. Deep Learning in Food Science: Innovative Approaches for Predicting and Simulating Food-Derived Protein–Peptides. *Trends Food Sci. Technol.* **2025**, *164*, 105216. [CrossRef]
39. Chen, T.; Ma, J.; Sheng, Y.; Cao, S.; Liu, H.; Yan, J.; Yang, H.; Qi, X.; Shi, Q. Preparation, Purification, Identification and Molecular Dynamics Simulation of Antioxidant Peptides from Mackerel (*Pneumatophorus japonicus*). *Food Biosci.* **2026**, *80*, 108954. [CrossRef]
40. Lu, J.; Shi, P.; Cao, Y.; Shi, B.; Shen, H.; Zhao, S.; Gao, Y.; Chi, H.; Wang, L.; Shi, Y. Isolation and Purification of Novel Antioxidant Peptides from Mussel (*Mytilus edulis*) Prepared by Marine *Bacillus velezensis* Z-1 Protease. *Mar. Drugs* **2025**, *23*, 294. [CrossRef] [PubMed]
41. Zhang, S.Y.; Zhao, G.X.; Suo, S.K.; Wang, Y.M.; Chi, C.F.; Wang, B. Purification, Identification, Activity Evaluation, and Stability of Antioxidant Peptides from Alcalase Hydrolysate of Antarctic Krill (*Euphausia superba*) Proteins. *Mar. Drugs* **2021**, *19*, 347. [CrossRef] [PubMed]
42. Wu, J.; Wang, X.; Qiao, K.; Pan, N.; Chen, X.; Liu, Z.; Chen, Y. Screening and Antioxidant Activities Evaluation of Peptides from Abalone (*Haliotis discus hannai* Ino). *Food Sci. Nutr.* **2025**, *13*, e70028. [CrossRef] [PubMed]
43. Hesamzadeh, P.; Seif, A.; Mahmoudzadeh, K.; Ganjali Koli, M.; Mostafazadeh, A.; Nayeri, K.; Mirjafary, Z.; Saeidian, H. De Novo Antioxidant Peptide Design via Machine Learning and DFT Studies. *Sci. Rep.* **2024**, *14*, 6473. Correction in *Sci. Rep.* **2026**, *16*, 17341. https://doi.org/10.1038/s41598-026-55147-y. [CrossRef] [PubMed]
44. La Paglia, L.; Vazzana, M.; Mauro, M.; Dumas, F.; Urso, A.; Simon, S.; Drahos, L.; Vizzini, A. Identification of Antioxidant and Anti-Inflammatory Activity of Sea Cucumber (*Holothuria tubulosa*) Active Peptides by a Combined Approach of Omics Data and Bioinformatics Analysis. *Mar. Drugs* **2026**, *24*, 158. [CrossRef] [PubMed]
45. Lassoued, I.; Mora, L.; Nasri, R.; Jridi, M.; Toldrá, F.; Aristoy, M.C.; Barkia, A.; Nasri, M. Characterization and Comparative Assessment of Antioxidant and ACE Inhibitory Activities of Thornback Ray Gelatin Hydrolysates. *J. Funct. Foods* **2015**, *13*, 225–238. [CrossRef]
46. Qiu, Y.T.; Wang, Y.M.; Yang, X.R.; Zhao, Y.Q.; Chi, C.F.; Wang, B. Gelatin and Antioxidant Peptides from Gelatin Hydrolysate of Skipjack Tuna (*Katsuwonus pelamis*) Scales: Preparation, Identification and Activity Evaluation. *Mar. Drugs* **2019**, *17*, 565. [CrossRef] [PubMed]
47. Chen, W.; Hong, Y.; Jia, Z.; Huang, G. Purification and Identification of Antioxidant Peptides from Hydrolysates of Large Yellow Croaker (*Pseudosciaena crocea*) Scales. *Trans. ASABE* **2020**, *63*, 289–294. [CrossRef]
48. Duy, H.A.; Srisongkram, T. Accurate Structure–Activity Relationship Prediction of Antioxidant Peptides Using a Multimodal Deep Learning Framework. *J. Cheminform.* **2025**, *17*, 166. [CrossRef] [PubMed]
49. Ma, Y.; Zhang, D.; Liu, M.; Li, Y.; Lv, R.; Li, X.; Wang, Q.; Ren, D.; Wu, L.; Zhou, H. Identification of Antioxidant Peptides Derived from Tilapia (*Oreochromis niloticus*) Skin and Their Mechanism of Action by Molecular Docking. *Foods* **2022**, *11*, 2576. [CrossRef] [PubMed]
50. Huang, H.; Cen, J.; Yang, D.; Li, L.; Li, C.; Yang, X.; Wang, Y.; Hu, X.; Wang, J.; Cai, Q. Isolation and Characterization of Antioxidant Peptides from Oyster (*Crassostrea rivularis*) Protein Enzymatic Hydrolysates. *Food Sci. Nutr.* **2023**, *11*, 261–273. [CrossRef] [PubMed]
51. Wu, R.; Wu, C.; Liu, D.; Yang, X.; Huang, J.; Zhang, J.; Liao, B.; He, H. Antioxidant and Anti-freezing Peptides from Salmon Collagen Hydrolysate Prepared by Bacterial Extracellular Protease. *Food Chem.* **2018**, *248*, 346–352. [CrossRef] [PubMed]
52. Sun, K.L.; Gao, M.; Wang, Y.Z.; Li, X.R.; Wang, P.; Wang, B. Antioxidant Peptides from Protein Hydrolysate of Marine Red Algae *Eucheuma cottonii*: Preparation, Identification, and Cytoprotective Mechanisms on H_2O_2 Oxidative Damaged HUVECs. *Front. Microbiol.* **2022**, *13*, 791248. [CrossRef] [PubMed]
53. Jegani, K.T.; Balde, A.; Nazeer, R.A. A Review on Anti-Inflammatory and Antioxidant Peptides Derived from Marine Organisms: Mechanism of Action and Therapeutic Applications. *Food Biosci.* **2025**, *63*, 105745. [CrossRef]
54. Sampath Kumar, N.S.; Nazeer, R.A.; Jaiganesh, R. Purification and Identification of Antioxidant Peptides from the Skin Protein Hydrolysate of Two Marine Fishes, Horse Mackerel (*Magalaspis cordyla*) and Croaker (*Otolithes ruber*). *Amino Acids* **2012**, *42*, 1641–1649. [CrossRef] [PubMed]

55. Wang, B.; Li, L.; Chi, C.F.; Ma, J.H.; Luo, H.Y.; Xu, Y.F. Purification and Characterisation of a Novel Antioxidant Peptide Derived from Blue Mussel (*Mytilus edulis*) Protein Hydrolysate. *Food Chem.* **2013**, *138*, 1713–1719. [CrossRef] [PubMed]
56. Park, S.Y.; Kim, Y.S.; Ahn, C.B.; Je, J.Y. Partial Purification and Identification of Three Antioxidant Peptides with Hepatoprotective Effects from Blue Mussel (*Mytilus edulis*) Hydrolysate by Peptic Hydrolysis. *J. Funct. Foods* **2016**, *20*, 88–95. [CrossRef]
57. Oh, Y.; Ahn, C.B.; Cho, W.H.; Yoon, N.Y.; Je, J.Y. Anti-osteoporotic Effects of Antioxidant Peptides PIISVYWK and FSVVPSPK from *Mytilus edulis* on Ovariectomized Mice. *Antioxidants* **2020**, *9*, 866. [CrossRef] [PubMed]
58. Yang, X.R.; Qiu, Y.T.; Zhao, Y.Q.; Chi, C.F.; Wang, B. Purification and Characterization of Antioxidant Peptides Derived from Protein Hydrolysate of the Marine Bivalve Mollusk *Tergillarca granosa*. *Mar. Drugs* **2019**, *17*, 251. [CrossRef] [PubMed]
59. Umayaparvathi, S.; Arumugam, M.; Meenakshi, S.; Dräger, G.; Kirschning, A.; Balasubramanian, T. Purification and Characterization of Antioxidant Peptides from Oyster (*Saccostrea cucullata*) Hydrolysate and the Anticancer Activity of Hydrolysate on Human Colon Cancer Cell Lines. *Int. J. Pept. Res. Ther.* **2014**, *20*, 231–243. [CrossRef]
60. Yuan, G.; Li, W.; Pan, Y.; Wang, C.; Chen, H. Shrimp Shell Wastes: Optimization of Peptide Hydrolysis and Peptide Inhibition of Alpha-Amylase. *Food Biosci.* **2018**, *25*, 52–60. [CrossRef]
61. Zhao, W.H.; Luo, Q.B.; Pan, X.; Chi, C.F.; Sun, K.L.; Wang, B. Preparation, Identification, and Activity Evaluation of Ten Antioxidant Peptides from Protein Hydrolysate of Swim Bladders of Miiuy Croaker (*Miichthys miiuy*). *J. Funct. Foods* **2018**, *47*, 503–511. [CrossRef]
62. Cai, S.Y.; Wang, Y.M.; Zhao, Y.Q.; Chi, C.F.; Wang, B. Cytoprotective Effect of Antioxidant Pentapeptides from the Protein Hydrolysate of Swim Bladders of Miiuy Croaker (*Miichthys miiuy*) Against H_2O_2-Mediated Human Umbilical Vein Endothelial Cell (HUVEC) Injury. *Int. J. Mol. Sci.* **2019**, *20*, 5425. [CrossRef] [PubMed]
63. Mendis, E.; Rajapakse, N.; Kim, S.K. Antioxidant Properties of a Radical-Scavenging Peptide Purified from Enzymatically Prepared Fish Skin Gelatin Hydrolysate. *J. Agric. Food Chem.* **2005**, *53*, 581–587. [CrossRef] [PubMed]
64. Sun, L.; Chang, W.; Ma, Q.; Zhuang, Y. Purification of Antioxidant Peptides by High Resolution Mass Spectrometry from Simulated Gastrointestinal Digestion Hydrolysates of Alaska Pollock (*Theragra chalcogramma*) Skin Collagen. *Mar. Drugs* **2016**, *14*, 186. [CrossRef] [PubMed]
65. Kim, H.S.; Kim, S.Y.; Fernando, I.P.S.; Sanjeewa, K.K.A.; Wang, L.; Lee, S.H.; Ko, S.C.; Kang, M.C.; Jayawardena, T.U.; Jeon, Y.J. Free Radical Scavenging Activity of the Peptide from the Alcalase Hydrolysate of the Edible Aquacultural Seahorse (*Hippocampus abdominalis*). *J. Food Biochem.* **2019**, *43*, e12833. [CrossRef] [PubMed]
66. Ding, D.; Du, B.; Zhang, C.; Zaman, F.; Huang, Y. Isolation and Identification of an Antioxidant Collagen Peptide from Skipjack Tuna (*Katsuwonus pelamis*) Bone. *RSC Adv.* **2019**, *9*, 27032–27041. [CrossRef] [PubMed]
67. Lassoued, I.; Mora, L.; Barkia, A.; Aristoy, M.C.; Nasri, M.; Toldrá, F. Bioactive Peptides Identified in Thornback Ray Skin's Gelatin Hydrolysates by Proteases from *Bacillus subtilis* and *Bacillus amyloliquefaciens*. *J. Proteom.* **2015**, *128*, 8–17. [CrossRef] [PubMed]
68. Anh, P.T.H.; Trang, H.P.; Thanh, B.D.; Trinh, N.T.N.; Thang, T.D.; Phuong, D.L.; Tuan, N.N.; Huyen, T.T. Antioxidant Capacity and Sequence of Peptides Derived from Oysters and Green Mussels in Vietnam. *Int. Food Res. J.* **2023**, *30*, 736–749. [CrossRef]
69. Chen, F.; Liu, H.S.; Yan, J.X.; Shi, Q.; Yang, H.; Cao, S.Q.; Qi, X.Y. Identification and Molecular Mechanism of Novel Antioxidant Peptides from Squid Skin Protein Hydrolysates: In Silico and In Vitro Analysis. *LWT* **2024**, *214*, 117081. [CrossRef]
70. Jin, H.X.; Xu, H.P.; Li, Y.; Zhang, Q.W.; Xie, H. Preparation and Evaluation of Peptides with Potential Antioxidant Activity by Microwave Assisted Enzymatic Hydrolysis of Collagen from Sea Cucumber *Acaudina molpadioides* Obtained from Zhejiang Province in China. *Mar. Drugs* **2019**, *17*, 169. [CrossRef] [PubMed]
71. Li, Y.; Li, J.; Lin, S.J.; Yang, Z.S.; Jin, H.X. Preparation of Antioxidant Peptide by Microwave- Assisted Hydrolysis of Collagen and Its Protective Effect Against H_2O_2-Induced Damage of RAW264.7 Cells. *Mar. Drugs* **2019**, *17*, 642. [CrossRef] [PubMed]
72. He, S.; Zhao, W.; Chen, X.; Li, J.; Zhang, L.; Jin, H. Ameliorative Effects of Peptide Phe–Leu–Ala–Pro on Acute Liver and Kidney Injury Caused by CCl_4 via Attenuation of Oxidative Stress and Inflammation. *ACS Omega* **2022**, *7*, 44796–44803. [CrossRef] [PubMed]
73. Zhang, Z.; Wang, J.; Deng, Y.; Wang, Y.; Dou, P.; Fan, H.; Zeng, X.; Fan, X.; Zhang, L.; Liu, H.; et al. Screening and Identification of Antioxidant Peptides from Sea Cucumber Gonad Proteins and Their Activation of Superoxide Dismutase. *Foods* **2025**, *14*, 3848. [CrossRef] [PubMed]
74. Hu, X.; Liu, J.; Li, J.; Song, Y.; Chen, S.; Zhou, S.; Yang, X. Preparation, Purification, and Identification of Novel Antioxidant Peptides Derived from *Gracilariopsis lemaneiformis* Protein Hydrolysates. *Front. Nutr.* **2022**, *9*, 971419. [CrossRef] [PubMed]
75. Xu, F.; Zhang, Y.; Qiu, Y.; Yang, F.; Liu, G.; Dong, X.; Chen, G.; Cao, C.; Zhang, Q.; Zhang, S.; et al. Three Novel Antioxidant Peptides Isolated from C-Phycocyanin Against H_2O_2-Induced Oxidative Stress in Zebrafish via Nrf2 Signaling Pathway. *Front. Mar. Sci.* **2022**, *9*, 1098091. [CrossRef]
76. Mirzaee, Z.; Gulcin, İ. Antioxidant Peptides in Focus: A Structural and Predictive Analysis of Radical Scavenging Mechanisms. *Int. J. Pept. Res. Ther.* **2026**, *32*, 2. [CrossRef]

77. Lv, X.; Yuan, S.; Sun, Y.; Zhang, Y.; Yang, W.; Xu, H.; Yan, W.; Bai, Q.; Bai, F.; Cui, F.; et al. Isolation and Identification of a Novel Antioxidant Peptide from Fermented Sea Cucumber (*Stichopus japonicus*) Intestine and Its Protective Effects on HepG2 Cells from Oxidative Damage. *J. Agric. Food Chem.* **2025**, *73*, 9062–9075. [CrossRef] [PubMed]
78. Mi, R.; Fu, Z.; Jiang, J.; Gao, S.; Guan, X.; Wang, X.; Zhou, Z. Sea Cucumber Viscera Processed by Protease Hydrolysis Combined with Cordyceps militaris Fermentation Protect Caco-2 Cells Against Oxidative Damage via Enhancing Antioxidant Capacity, Activating Nrf2/HO-1 Pathway and Improving Cell Metabolism. *Antioxidants* **2024**, *13*, 988. [CrossRef] [PubMed]
79. Vijayan, D.K.; Sreerekha, P.R.; Dara, P.K.; Ganesan, B.; Mathew, S.; Anandan, R.; Ravisankar, C.N. Antioxidant Defense of Fish Collagen Peptides Attenuates Oxidative Stress in Gastric Mucosa of Experimentally Ulcer-Induced Rats. *Cell Stress Chaperones* **2022**, *27*, 45–54. [CrossRef] [PubMed]
80. Lin, Q.; Guo, Y.; Li, J.; He, S.; Chen, Y.; Jin, H. Antidiabetic Effect of Collagen Peptides from *Harpadon nehereus* Bones in Streptozotocin-Induced Diabetes Mice by Regulating Oxidative Stress and Glucose Metabolism. *Mar. Drugs* **2023**, *21*, 518. [CrossRef] [PubMed]
81. Alghamdi, A.A.; Al-Hazmi, A.; Almalki, A.A.; Alsubaihi, A.A.; Anagreyyah, S.A.; Qasem, A.H.; Anajirih, N.A.; Allahyani, M.; Alyamani, R.A.; Albanghali, M.A.; et al. Antioxidant Activity Derived from Marine Green-Lipped Mussel *Perna canaliculus* Extracts in Mice. *BioMed Res. Int.* **2021**, *2021*, 1622270. [CrossRef] [PubMed]
82. Cai, X.; Chen, S.; Liang, J.; Tang, M.; Wang, S. Protective Effects of Crimson Snapper Scales Peptides Against Oxidative Stress on *Drosophila melanogaster* and the Action Mechanism. *Food Chem. Toxicol.* **2021**, *148*, 111965. [CrossRef] [PubMed]
83. Yang, F.; Yang, Y.; Xiao, D.; Kim, P.; Lee, J.; Jeon, Y.J.; Wang, L. Anti-Photoaging Effects of Antioxidant Peptide from Seahorse (*Hippocampus abdominalis*) in In Vivo and In Vitro Models. *Mar. Drugs* **2024**, *22*, 471. [CrossRef] [PubMed]
84. De Luca, C.; Mikhal'chik, E.V.; Suprun, M.V.; Papacharalambous, M.; Truhanov, A.I.; Korkina, L.G. Skin Antiageing and Systemic Redox Effects of Supplementation with Marine Collagen Peptides and Plant-Derived Antioxidants: A Single-Blind Case-Control Clinical Study. *Oxid. Med. Cell. Longev.* **2016**, *2016*, 4389410. [CrossRef] [PubMed]
85. Huang, J.; Chen, C.; Zhang, M.; Li, J.; Wang, R.; Wang, Y.; Zhang, J.; Chen, Q. Oral Fish Collagen Peptide Complex Enhances Skin Rejuvenation and Systemic Health Biomarkers: A 90 Day Prospective Observational Study. *J. Cosmet. Dermatol.* **2026**, *25*, e70841. [CrossRef] [PubMed]
86. Myung, S.K.; Park, Y. Effects of Collagen Supplements on Skin Aging: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Am. J. Med.* **2025**, *138*, 1264–1277. [CrossRef] [PubMed]
87. Chakniramol, S.; Wierschem, A.; Cho, M.G.; Bashir, K.M.I. Physiological and Clinical Aspects of Bioactive Peptides from Marine Animals. *Antioxidants* **2022**, *11*, 1021. [CrossRef] [PubMed]
88. Ichikawa, S.; Morifuji, M.; Ohara, H.; Matsumoto, H.; Takeuchi, Y.; Sato, K. Hydroxyproline-Containing Dipeptides and Tripeptides Quantified at High Concentration in Human Blood after Oral Administration of Gelatin Hydrolysate. *Int. J. Food Sci. Nutr.* **2010**, *61*, 52–60. [CrossRef] [PubMed]
89. Okagu, I.U.; Udenigwe, C.C. Transepithelial Transport and Cellular Mechanisms of Food-Derived Antioxidant Peptides. *Heliyon* **2022**, *8*, e10861. [CrossRef] [PubMed]
90. Hamadou, M.; Mishra, S.K.; Abubakar, A.M.; Başaran, B.; Martin Alain, M.M. From Bench to Bedside: Experimental Pharmacology Approaches to Overcome Bioavailability, Stability, and Translational Barriers of Bioactive Peptides from Natural Sources. *Front. Pharmacol.* **2026**, *17*, 1863016. [CrossRef] [PubMed]
91. Wang, Y.Z.; Zhao, Y.Q.; Wang, Y.M.; Zhao, W.H.; Wang, P.; Chi, C.F.; Wang, B. Antioxidant Peptides from Antarctic Krill (*Euphausia superba*) Hydrolysate: Preparation, Identification and Cytoprotection on H_2O_2-Induced Oxidative Stress. *J. Funct. Foods* **2021**, *86*, 104701. [CrossRef]
92. Future Market Insights. Marine Peptide Market: Global Industry Analysis and Opportunity Assessment. 2036. Available online: https://www.futuremarketinsights.com/reports/marine-peptide-market (accessed on 15 September 2026).
93. Fact.MR. Marine Peptides Market Forecast and Outlook 2025 to 2035. 2025. Available online: https://www.factmr.com/report/marine-peptides-market (accessed on 15 September 2026).
94. Whitaker, R.D.; Altintzoglou, T.; Lian, K.; Fernandez, E.N. Marine Bioactive Peptides in Supplements and Functional Foods—A Commercial Perspective. *Curr. Pharm. Des.* **2021**, *27*, 1353–1364. [CrossRef] [PubMed]
95. Keshavarz, B.; Rao, Q.; Jiang, X.; Hsieh, Y.H.P. Immunochemical Analysis of Pepsin-Digested Fish Tropomyosin. *Food Control* **2020**, *118*, 107427. [CrossRef]
96. Bai, T.L.; Han, X.Y.; Li, M.S.; Yang, Y.; Liu, M.; Ji, N.R.; Yu, C.C.; Lai, D.; Cao, M.J.; Liu, G.M. Effects of the Maillard Reaction on the Epitopes and Immunoreactivity of Tropomyosin, a Major Allergen in Chlamys nobilis. *Food Funct.* **2021**, *12*, 5096–5108. [CrossRef] [PubMed]
97. Garofalo, L.; Sala, M.; Focardi, C.; Pasqualetti, P.; Delfino, D.; D'Onofrio, F.; Droghei, B.; Pasquali, F.; Nicolini, V.; Galli, F.S.; et al. Monitoring of Cadmium, Lead, and Mercury Levels in Seafood Products: A Ten-Year Analysis. *Foods* **2025**, *14*, 451. [CrossRef] [PubMed]

98. Galinytė, D.; Balčiūnaitė-Murzienė, G.; Karosienė, J.; Morudov, D.; Naginienė, R.; Baranauskienė, D.; Šulinskienė, J.; Kudlinskienė, I.; Savickas, A.; Savickienė, N. Determination of Heavy Metal Content: Arsenic, Cadmium, Mercury, and Lead in Cyano-Phycocyanin Isolated from the Cyanobacterial Biomass. *Plants* **2023**, *12*, 3150. [CrossRef] [PubMed]
99. Sohaib, M.; Anjum, F.M.; Sahar, A.; Arshad, M.S.; Rahman, U.U.; Imran, A.; Hussain, S. Antioxidant Proteins and Peptides to Enhance the Oxidative Stability of Meat and Meat Products: A Comprehensive Review. *Int. J. Food Prop.* **2017**, *20*, 2581–2593. [CrossRef]
100. Varona, E.; García-Moreno, P.J.; Gregersen Echers, S.; Olsen, T.H.; Marcatili, P.; Guardiola, F.; Overgaard, M.T.; Hansen, E.B.; Jacobsen, C.; Yesiltas, B. Antioxidant Peptides from Alternative Sources Reduce Lipid Oxidation in 5% Fish Oil-in-Water Emulsions (pH 4) and Fish Oil-Enriched Mayonnaise. *Food Chem.* **2023**, *426*, 136498. [CrossRef] [PubMed]
101. Idowu, A.T.; Benjakul, S. Bitterness of Fish Protein Hydrolysate and Its Debittering Prospects. *J. Food Biochem.* **2019**, *43*, e12978. [CrossRef] [PubMed]
102. Nwachukwu, I.D.; Sarteshnizi, R.A.; Udenigwe, C.C.; Aluko, R.E. A Concise Review of Current In Vitro Chemical and Cell-Based Antioxidant Assay Methods. *Molecules* **2021**, *26*, 4865. [CrossRef] [PubMed]
103. Aguilar-Toalá, J.E.; Quintanar-Guerrero, D.; Liceaga, A.M.; Zambrano-Zaragoza, M.L. Encapsulation of Bioactive Peptides: A Strategy to Improve the Stability, Protect the Nutraceutical Bioactivity and Support Their Food Applications. *RSC Adv.* **2022**, *12*, 6449–6458. [CrossRef] [PubMed]
104. Auwal, S.M.; Zarei, M.; Tan, C.P.; Basri, M.; Saari, N. Improved In Vivo Efficacy of Anti-hypertensive Biopeptides Encapsulated in Chitosan Nanoparticles Fabricated by Ionotropic Gelation on Spontaneously Hypertensive Rats. *Nanomaterials* **2017**, *7*, 421. [CrossRef] [PubMed]
105. Ünlüsayin, M.; Ceylan, Z.; Balci, B.A.; Arslan, M.N. Marine Bio-peptides Integrated with Foods Supported by a Nanotechnology Approach. *Int. J. Food Sci. Technol.* **2026**, *61*, vvag123. [CrossRef]

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