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The Antihypertensive Potential of Seaweed-Derived Bioactive Compounds and Peptides: A Systematic Review

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ABSTRACT

Hypertension remains a major global health burden and an important risk factor for cardiovascular and renal diseases. Although conventional antihypertensive drugs are effective, their long-term use is often associated with adverse effects, prompting the search for safer natural alternatives. Seaweeds have attracted increasing attention as sources of bioactive compounds and peptides with potential antihypertensive properties. This systematic review evaluated the antihypertensive potential of seaweed-derived bioactives based on in vitro and in vivo studies published between 2015 and 2025. Literature was retrieved from the Scopus database following PRISMA guidelines. The findings indicate that fucoxanthin, phlorotannins (e.g., dieckol), diphlorethohydroxycarmalol (DPHC), sulfated polysaccharides, and bioactive peptides exert antihypertensive effects through multiple mechanisms, including modulation of the renin–angiotensin–aldosterone system (RAAS), enhancement of nitric oxide bioavailability, suppression of oxidative stress, and possible regulation of renal sodium balance and gut microbiota. Overall, seaweed-derived bioactives are promising candidates for functional foods and nutraceuticals for hypertension management, although clinical studies are still required to confirm their efficacy, safety, and bioavailability.

1 | Introduction

Hypertension is a major non-communicable disease contributing significantly to global mortality, primarily as a leading risk factor for stroke, cardiovascular disease, and chronic kidney disease [1–3]. According to the World Health Organization (WHO), approximately 1.28 billion adults aged 30–79 years are affected, with nearly two-thirds residing in developing countries [4, 5]. Hypertension is multifactorial, involving genetic, dietary, lifestyle, and psychological factors [6–9]. Management primarily relies on pharmacological therapies, including angiotensin-converting enzyme (ACE) inhibitors, diuretics, angiotensin receptor blockers (ARBs), β-blockers, and calcium channel blockers [10–13]. Although effective, long-term use is associated with adverse effects such as electrolyte imbalance, dehydration, renal dysfunction, fatigue, dizziness, allergic reactions, and potential kidney and liver damage [14, 15]. These limitations have driven interest in safer, sustainable alternatives, particularly natural product-based therapies [16–20].

Seaweeds are promising antihypertensive sources due to their composition of primary metabolites (carbohydrates, proteins, and minerals) and secondary metabolites [21–27]. These include saponins, alkaloids, sterols, terpenoids, phenolics, and flavonoids, which contribute to hypertension prevention [28–31]. High phenolic content supports strong antioxidant activity; for

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example, *Durvillaea* sp. (Phaeophyceae) contains 23.1 mg GAE/g phenolics [32]; while *Phacelocarpus peperocarpos* (Rhodophyta) contains 7.5 mg GAE/g with antioxidant activity of 2.66 mg TE/g [33]. Similarly, *Kappaphycus alvarezii* (Rhodophyta) contains notable levels of polyphenols, flavonoids, tannins, saponins, and alkaloids [34]. These compounds exhibit diverse biological activities, including antihypertensive, antioxidant, anti-inflammatory, antimicrobial, neuroprotective, chemoprotective, immunomodulatory, and hepatoprotective effects [28, 29, 35–42].

Seaweeds are also rich in bioactive peptides with antihypertensive potential [43–46]. Peptides from *Gracilaria gracilis*, *Ulva lactuca*, and *Ulva* spp. (Chlorophyta) exhibit antioxidant activity and inhibit ACE and dipeptidyl peptidase IV (DPP-IV) [47]. Peptides from *Pyropia vietnamensis* and *Gracilaria changii* (Rhodophyta) also show antihypertensive effects via ACE inhibition [48, 49]. Polysaccharides including fucoidan, alginate, carrageenan, ulvan, β-glucan, and chitosan reduce angiotensin II, nitric oxide imbalance, and inflammation [23, 50]; while carrageenan exhibits antioxidant and ACE inhibitory properties [51]. Overall, these bioactives act through ACE inhibition, enhanced nitric oxide (NO) bioavailability, and oxidative stress suppression [52–54, 21, 55, 56].

Despite these advances, most existing studies focus on single mechanisms, chiefly ACE inhibition and antioxidant activity, which do not capture the complex, interconnected nature of hypertension. Blood pressure regulation instead depends on the coordinated activity of several systems, including the renin–angiotensin–aldosterone system (RAAS), endothelial nitric oxide signaling, renal sodium handling, the sympathetic nervous system, and the gut–cardiovascular axis, yet an integrative framework linking these pathways to seaweed bioactives is still lacking. This review therefore examines the antihypertensive effects of seaweed-derived bioactive compounds and peptides from a systems-level perspective, synthesizing molecular, cellular, and physiological evidence into a multi-target mechanistic framework for how these bioactives may influence blood pressure.

2 | Method

The researchers conducted a systematic review study that used PRISMA guidelines to establish transparent and reproducible research according to [57]. The researchers conducted a complete literature search using the Scopus database to identify relevant studies published between 2015 and 2025. Scopus was selected as the primary source because of its broad, multidisciplinary coverage of peer-reviewed biomedical and life-science literature; reliance on a single database is acknowledged as a limitation of this review (see Conclusion). The search strategy used the following keywords: ((“seaweed” or “macroalga” or “alga”) and (“antihypertensive” or “blood pressure” or “hypertension”) and (“mechanism” or “molecular mechanism” or “ACE inhibition”) and (“placebo” or “control” or “comparison”)). The terms “placebo” and “comparison” were included to help capture studies with controlled experimental designs; although this broadened the initial record count, all retrieved records were subsequently filtered against the PICO-based eligibility criteria described below, so the final set of included studies was not affected. Articles were screened according to inclusion and exclusion criteria based on the PICO framework. The Scopus search yielded a total of 577 records. After removing three duplicate records, 574 records were screened, of which 384 were excluded at the title/abstract stage. The remaining 190 full-text articles were assessed for eligibility, and 174 were excluded for not meeting the inclusion criteria. A total of 16 studies were ultimately included in the systematic review, as presented in Figure 1.

Researchers extracted data about study design, seaweed species, bioactive compounds, mechanisms of action, and antihypertensive outcomes through independent data extraction. The researchers found this limitation affected their results because it restricted their ability to apply findings to human populations. The PICO framework served as the basis for establishing both inclusion and exclusion criteria. The study selected only those research works that studied bioactive compounds from seaweed or seaweed peptides that produced antihypertensive results. The study removed research works that did not assess blood pressure and related measurements, contained non-English content or had insufficient research design standards (Table 1).

3 | Results and Discussion

3.1 | Search Results

The researchers examined selected studies to find patterns between antihypertensive effects and bioactive compounds and their associated mechanisms. The researchers conducted a literature search through the Scopus database, which led to a screening process that applied predetermined inclusion criteria connected to the review subject (Figure 1 and Table 1). The initial search produced 577 articles, which the researchers identified through this query: ((“seaweed” or “macroalga” or “alga”) and (“antihypertensive” or “blood pressure” or “hypertension”) and (“mechanism” or “molecular mechanism” or “ACE inhibition”) and (“placebo” or “control” or “comparison”). The screening process resulted in the removal of 561 articles because they contained irrelevant content, duplicate information, or did not satisfy the predefined inclusion standards. The researchers selected 16 articles, which included both in vitro and in vivo studies about the antihypertensive properties of seaweed. The systematic review used these selected studies as its base material.

3.2 | Antihypertensive Activity of Seaweed: A Review Based on In Vitro, In Vivo, and In Silico Study Designs (2015–2025)

The total number of studies listed in Table 2 exceeds the actual study count because some research studies tested multiple seaweed species together with their experimental models. Table 2 summarizes the antihypertensive activity of various seaweed species evaluated using in vitro, in vivo, and in silico approaches between 2015 and 2025. The dataset shows that every seaweed species included in this review was reported to exhibit measurable antihypertensive activity in vitro and/or in vivo; however, the strength of this evidence differs across species. Most species have so far been examined in only a single study, so their antihypertensive potential should be considered preliminary, whereas a smaller subset described in the following paragraph

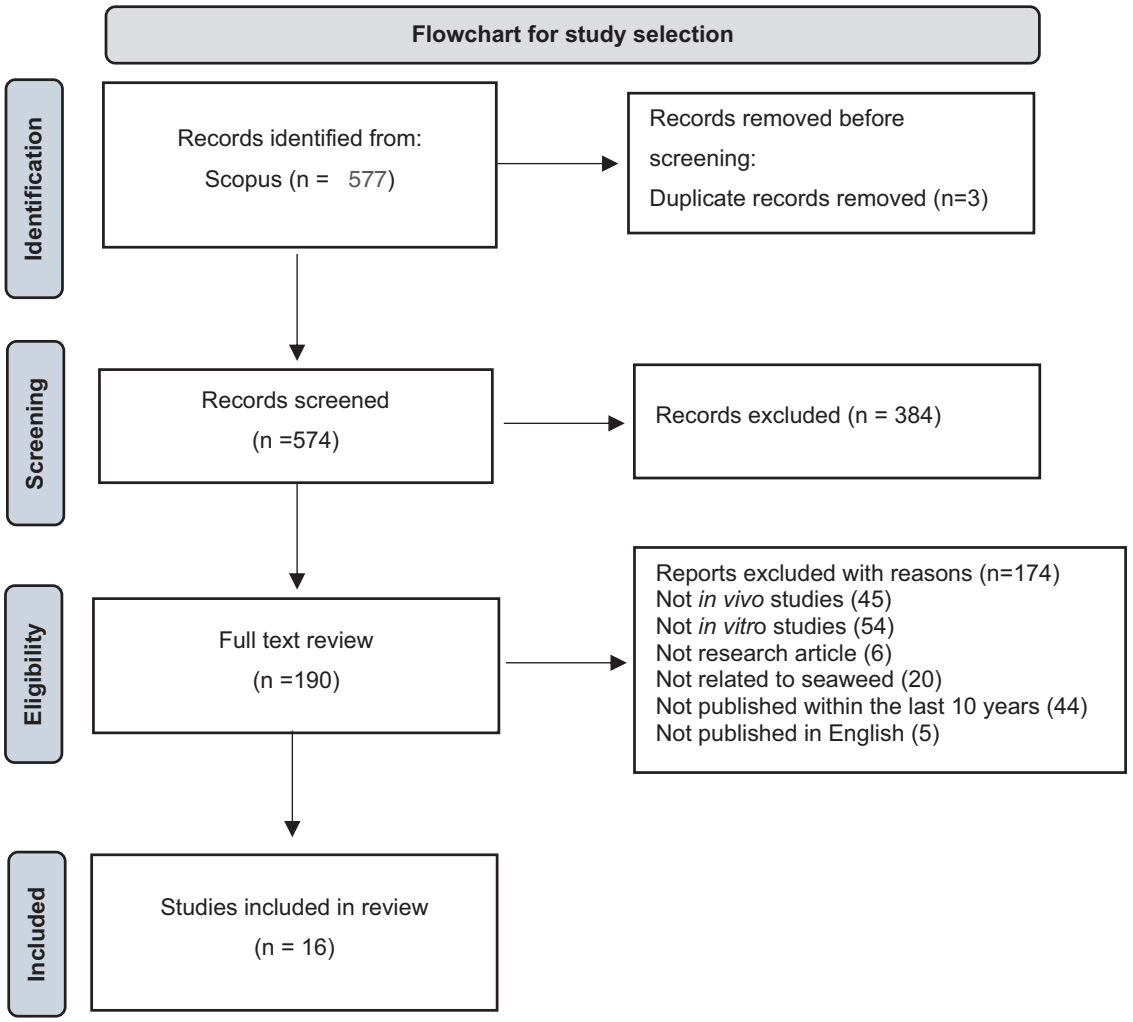


FIGURE 1 | PRISMA flow diagram of the study selection process.

TABLE 1 | Eligibility criteria of included studies based on participants, intervention, comparator, and outcomes (PICO).

Inclusion	Exclusion
P (Population): • In vitro and in vivo experimental studies *I (Intervention)*: • Bioactive compounds and peptides derived from *seaweed* *C (Comparison)*: • *Compared* with untreated control groups or standard antihypertensive treatments *O (Outcome)*: • Reduction in blood pressure	• Studies that do not involve seaweed-derived compounds or peptides as the intervention. • In vitro or in vivo studies that do not measure blood pressure or related indicators. • Articles published in languages other than English. • Studies with weak methodological design, such as case reports or invalid observational studies.

has been evaluated across multiple studies and experimental models and therefore offers comparatively stronger support. In vitro assays remain the most common initial screening approach, focusing mainly on ACE-inhibitory and antioxidant activity, while a growing number of more recent studies have incorporated in vivo models, reflecting a shift toward evidence with greater physiological relevance. Collectively, these patterns point to a promising but still uneven evidence base for the antihypertensive potential of seaweed-derived bioactives.

Several species, including *A. esculenta* (Phaeophyceae), *U. lactuca* (Chlorophyta), *P. palmata*, and *G. lemaneiformis* (Rhodophyta), have been evaluated across multiple experimental designs. This cross-validation strengthens the reliability of their antihypertensive effects and suggests consistent bioactivity across different biological systems. Such reproducibility is a critical indicator for further development into functional or therapeutic applications. More recent studies have increasingly incorporated in vivo models, particularly for species such as *S. wightii* and *E. cava*

TABLE 2 | Antihypertensive activity of seaweed species based on in vitro, in vivo, and in silico studies (2015–2025).

No.	Seaweeds	Study Design	Biological activity	Year	Reference
1	*Alaria esculenta* (Phaeophyceae)	In vitro	Antihypertensive activity	2025	[58]
2	*Ulva lactuca* (Chlorophyta)	In vitro	Antihypertensive activity	2025	[58]
3	*Palmaria palmata* (Rhodophyta)	In vitro	Antihypertensive activity	2025	[58]
4	*Ulva prolifera* (Chlorophyta)	In vitro	Antihypertensive activity	2024	[59]
5	*Valonia aegagropila* (Chlorophyta)	In vitro	Antihypertensive activity	2024	[60]
6	*Chaetomorpha linum* (Chlorophyta)	In vitro	Antihypertensive activity	2024	[60]
7	*Sargassum wightii* (Phaeophyceae)	In vivo	Antihypertensive activity	2023	[61]
8	*Gracilariopsis lemaneiformis* (Rhodophyta)	In vitro	Antihypertensive activity	2022	[62]
9	*Ecklonia cava* (Phaeophyceae)	In vitro and in vivo	Antihypertensive activity	2022	[63]
10	*Ishige okamurae* (Phaeophyceae)	In vitro and in vivo	Antihypertensive activity	2021	[64]
11	*Sargassum macclurei* (Phaeophyceae)	In vivo	Antihypertensive activity	2020	[65]
12	*Sarconema filiforme* (Rhodophyta)	In vivo	Antihypertensive activity	2020	[66]
13	*Ulva intestinalis* (Chlorophyta)	In vitro	Antihypertensive activity	2019	[67]
14	*Ulva lactuca* (Chlorophyta)	In vitro and in silico	Antihypertensive activity	2019	[68]
15	*Kappaphycus alvarezii* (Rhodophyta)	In vivo	Antihypertensive activity	2018	[69]
16	*Gracilaria opuntia* (Rhodophyta)	In vivo	Antihypertensive activity	2018	[69]
17	*Gracilariopsis lemaneiformis* (Rhodophyta)	In vivo	Antihypertensive activity	2018	[70]
18	*Fucus spiralis* L. (Phaeophyceae)	In vitro	Antihypertensive activity	2018	[71]
19	*Kappaphycus alvarezii* (Rhodophyta)	In vivo	Antihypertensive activity	2017	[72]
20	*Fucus distichus* (Phaeophyceae)	In vitro	Antihypertensive activity	2017	[73]

(Phaeophyceae), which demonstrate significant reductions in systolic and diastolic blood pressure. This trend highlights a shift from exploratory screening toward preclinical validation, emphasizing the therapeutic relevance of these species. In addition, although still limited, the integration of in silico approaches represents an emerging trend in seaweed research. Computational studies provide insights into molecular interactions, particularly ligand–enzyme binding mechanisms, which complement experimental findings and support mechanism-based drug discovery.

Overall, the data indicate a clear research progression from in vitro screening to in vivo validation, with emerging support from in silico analysis. This multi-level approach strengthens the evidence base for the antihypertensive potential of seaweed and underscores its promise for future development as a functional or therapeutic agent.

3.3 | Role of Seaweed-Derived Bioactive Compounds as Antihypertensive Agents

Seaweed-derived bioactive compounds have gained increasing attention due to their wide applications in food, nutraceutical, pharmaceutical, and cosmetic industries [35–40]. These compounds demonstrate multiple biological functions, which include antioxidant activity, anti-inflammatory activity, antimicrobial activity, anticancer activity, and antihypertensive activity [56]. Advanced studies through laboratory experiments and live organism testing have proven that different seaweed species, including *S. wightii, E. cava, I. okamurae, S. filiforme, K. alvarezii, F. spiralis*, and *F. distichus* possess bioactive substances reported to display antihypertensive activity (Table 3).

The research studies show that seaweed-based substances create blood pressure-lowering effects through mechanisms that operate on multiple biological systems including vascular systems and oxidative pathways and inflammatory pathways. The mechanisms of this system can be divided into four main functional pathways which operate as separate entities: (i) inhibition of the RAAS, (ii) enhancement of endothelial nitric oxide (NO) production, (iii) suppression of oxidative stress, and (iv) modulation of inflammatory and metabolic pathways. Within the RAAS pathway, several compounds act as ACE inhibitors. Fucoxanthin from *S. wightii* has been shown to reduce both systolic and diastolic blood pressure in vivo through ACE inhibition and attenuation of hyperglycemia-induced oxidative stress [61]. Similarly, phenolic compounds from *Fucus spiralis* and *K.alvarezii* demonstrate ACE inhibitory activity, contributing to reduced angiotensin II formation and vasoconstriction [69, 71].

Beyond RAAS inhibition, enhancement of endothelial function represents a second key mechanism. Diphlorethohydroxycarmalol (DPHC) isolated from *I. okamurae* increases nitric oxide (NO) production via activation of the PI3K/Akt/eNOS pathway,

TABLE 3 | Bioactive compounds from seaweeds and their antihypertensive mechanisms.

No.	Seaweeds	Bioactive compounds	Type Mechanism	Mechanism of the antihypertensive	Year	Reference
1	*S. wightii* (Phaeophyceae)	Fucoxanthin	Dual	↓ ACE-1; ↓ Oxidative stress	2023	[61]
2	*E. cava* (Phaeophyceae)	Phlorotannins (dieckol)	Dual	↑ PGC-1α/ NRF2/ SIRT3 and ↑ SOD2	2022	[63]
3	*I. okamurae* (Phaophyceae)	Diphlorethohydroxycarmalol	Dual	↑ PI3K/Akt/eNOS → ↑ NO, ↓ Ca^{2+}	2021	[64]
4	*S. filiforme* (Rhodophyta)	Polysaccharides (Carrageenan)	Single	↓ systolic blood	2020	[66]
5	*K. alvarezii* (Rhodophyta)	Sulfated polygalactans	Single	↓ ACE-1	2018	[69]
6	*F. spiralis* (Phaeophyceae)	Phenolic	Single	↓ ACE-1	2018	[71]
7	*K. alvarezii* (Rhodopohyta)	Carrageenan, phenolics, and flavonoids	Single	↓ Oxidative stress	2017	[72]
8	*F. distichus* (Phaeophyceae)	fucoidan/ polyphenols	Dual	↓ inflammation and Oxidative stress	2017	[73]

while also modulating intracellular calcium levels to promote vascular relaxation [64]. This mechanism directly addresses endothelial dysfunction, a central feature of hypertension. In addition, phlorotannins such as dieckol and bieckol from *E. cava* have been reported to enhance NO bioavailability while simultaneously inhibiting ACE activity, demonstrating a dual mechanism of action [46, 74, 75].

Oxidative stress suppression emerges as a consistent and critical mechanism across multiple compounds. Phlorotannins from *E. cava* activate antioxidant pathways including PGC-1α, NRF2, SIRT3, and SOD2, thereby reducing reactive oxygen species (ROS) and restoring vascular homeostasis [63]. Similarly, fucoxanthin has been shown to reduce oxidative stress through inhibition of the HIF-1α–ROS axis [76]. These findings highlight that antioxidant activity is not merely supportive but central to antihypertensive effects. In addition to vascular mechanisms, polysaccharides such as carrageenan and fucoidan exhibit broader systemic effects. Carrageenan from *S. filiforme* and *K. alvarezii* has been shown to reduce blood pressure and oxidative stress in hypertensive models [66, 72]. Fucoidan from *F. distichus* and *S. fusiforme* demonstrates multi-functional activity by inhibiting ACE, enhancing NO production, and suppressing inflammation via the SIRT1/NLRP3 pathway [77, 73, 78]. Furthermore, modulation of immune responses, including regulation of T regulatory cells and inhibition of pro-inflammatory pathways, has been identified as an additional mechanism contributing to blood pressure reduction [79].

Emerging evidence also highlights the role of the gut–cardiovascular axis. Polysaccharides from *Saccharina japonica* (Phaeophyceae) have been shown to lower blood pressure by modulating gut microbiota composition, increasing beneficial bacteria such as *Bacteroides acidifaciens*, and enhancing short-chain fatty acid (SCFA) production and GLP-1 secretion [80]. This indicates that seaweed bioactives may influence systemic metabolic regulation beyond direct vascular effects, although this gut–cardiovascular mechanism is currently supported by a single study and should be regarded as preliminary until confirmed by further research. Phenolic and flavonoid compounds further reinforce the antihypertensive potential of seaweed. These compounds act as radical scavengers, reducing oxidative stress and preventing vascular damage [81, 21]. Their presence across multiple species, including *Ulva reticulata* and *Padina boergesenii*, suggests that antioxidant-driven vascular protection is a conserved mechanism among seaweed-derived metabolites [82, 83].

Collectively, these findings indicate that seaweed-derived bioactive compounds exert antihypertensive effects through integrated and synergistic mechanisms, rather than isolated pathways. Compounds with dual or multitarget activity such as fucoxanthin, phlorotannins, DPHC, and fucoidan demonstrate enhanced efficacy by simultaneously modulating RAAS, endothelial function, oxidative stress, and inflammatory pathways. This multipathway interaction supports the concept that seaweed bioactives represent promising candidates for the development of functional antihypertensive agents and nutraceutical interventions.

3.4 | Role of Seaweed-Derived Bioactive Peptides as Antihypertensive Agents

Recent years have witnessed a significant increase in research on seaweed-derived bioactive peptides, driven by growing interest in sustainable natural resources and functional foods [25, 84–87]. Seaweeds from red, brown, and green groups have been widely recognized as promising sources of bioactive peptides with diverse pharmacological activities, particularly antihypertensive effects [25, 88–90]. Evidence from multiple studies indicates that seaweed-derived peptides exhibit antihypertensive activity, primarily through ACE inhibition, although reported potencies (e.g., IC_{50} values) vary considerably across species and peptides. Peptides including PP from *P. palmata* and KAF from *U. prolifera* exhibit strong ACE inhibitory effects, which their low IC_{50} values demonstrate through their high binding affinity to the enzyme [58, 59]. The peptides VA and CL, which scientists extracted from *V. aegagropila* and *C. linum*, showed strong ACE inhibition,

TABLE 4 | Bioactive peptides derived from seaweeds and their antihypertensive mechanisms.

No.	Seaweeds	Bioactive peptides	ACE-1 inhibitors (IC_{50})	Type Mechanism	Mechanism of the antihypertensive	Year	Reference
1	*P. palmata*	Peptide PP	94.29 μg/mL	Single	↓ Blood pressure	2025	[58]
2	*U. prolifera*	Peptide KAF	0.63 μM	Dual	↓ Blood pressure	2024	[59]
3	*V. aegagropila*	Peptide VA	5.71 mg DW	Single	↓ ACE	2024	[60]
4	*C. linum*	Peptide CL	3.02 mg DW	Single	↓ ACE	2024	[60]
5	*G. lemaneiformis*	SFYYGK	6.45 μmoL/L	Single	↓ Blood pressure	2022	[62]
6	*G. lemaneiformis*	RLVPVPY	9.18 μmoL/L	Single	↓ Blood pressure	2022	[62]
7	*G. lemaneiformis*	YIGNNPAKG	11.23 μmoL/L	Single	↓ Blood pressure	2022	[62]
8	*S. maclurei*	RWDISQPY	72.24 μM	Dual	↓ Systolic blood and ↓diastolic blood; ↓Endothelin-1 (ET-1)	2020	[65]
9	*U. intestinalis*	FGMPLDR	219.35 μM	Single	↓ ACE	2019	[67]
10	*U. intestinalis*	MELVLR	236.85 μM	Single	↓ ACE	2019	[67]
11	*G. lemaneiformis*	FQIN [M(O)] CILR	64 μM	Dual	↓ Systolic blood and ↓diastolic blood	2018	[70]
12	*G. lemaneiformis*	TGAPCR	23.94 μM	Dual	↓ Systolic blood and ↓diastolic blood	2018	[69]

which provides additional proof that macroalgal peptides control the renin–angiotensin system [60].

The peptides SFYYGK, RLVPVPY, and YIGNNPAKG, which researchers extracted from *G. lemaneiformis*, show strong ACE inhibitory activity, which helps lower blood pressure according to study [61]. The FQIN[M(O)]CILR and TGAPCR peptides, which scientists discovered, demonstrate their ability to lower systolic and diastolic blood pressure through mechanisms that go beyond their ability to inhibit enzyme activity [69]. The *U. intestinalis* peptides FGMPLDR and MELVLR show moderate ACE inhibition, further supporting the presence of antihypertensive peptides in green macroalgae according to research findings [66]. The study results show that certain peptides possess multiple functional pathways for their biological activities.

The peptide RWDISQPY from *S. macclurei* not only inhibits ACE but also reduces endothelin-1 (ET-1), a potent vasoconstrictor, thereby enhancing its antihypertensive efficacy [64]. Similarly, peptides identified in *Porphyridium sp*. demonstrate anti-inflammatory activity through cyclooxygenase-1 (COX-1) inhibition, which may contribute indirectly to blood pressure regulation [90]. In addition, peptides derived from *L. digitata* (IGNNPAKGGLF and YIGNNPAKGGLF) further support the broad spectrum of antihypertensive potential found in marine peptides (Table 4) [91, 92].

From a mechanistic perspective, most seaweed-derived peptides act as competitive ACE inhibitors, interacting with the active site of the enzyme through hydrophobic and aromatic amino acid residues. This interaction prevents the formation of angiotensin II, thereby reducing vasoconstriction and lowering blood pressure. However, emerging evidence indicates that certain peptides exhibit multi-target activity. For example, KAF enhances nitric oxide (NO) production, improving endothelial function, while RWDISQPY suppresses ET-1, reducing vascular resistance. These dual or multifunctional mechanisms suggest that bioactive peptides may provide more comprehensive antihypertensive effects compared to single-target compounds. Overall, the findings highlight that seaweed-derived bioactive peptides contribute to blood pressure regulation through both single-target (ACE inhibition) and multi-target mechanisms involving endothelial modulation, vasoconstrictor suppression, and anti-inflammatory pathways. This multifunctional profile underscores their potential as promising candidates for the development of functional foods and therapeutic agents for hypertension management [25]. It should be noted, however, that most of the IC_{50} values reported in Table 4 were obtained from in vitro enzyme assays; the physiological relevance of these peptides depends on factors that were rarely addressed in the reviewed studies, including their bioavailability after oral intake, resistance to gastrointestinal digestion, and stability during food processing and storage. Until these factors are systematically evaluated, the in vitro potency of seaweed-derived peptides should not be assumed to translate directly into an equivalent effect in vivo.

3.5 | Heatmap Distribution of Bioactive Compounds and Peptides in Seaweed Sources

The heatmap (Figure 2) shows how bioactive compounds and peptides distribute among different seaweed species because the heatmap uses rows to show species and columns to display bioactive compounds. The table uses cells to show compound presence with 1 and absence with 0, while the total column presents the complete count of bioactive components found in each species. The system allows users to quickly compare different species and their various metabolic functions.

The heatmap analysis enables the identification of important patterns that emerge from the data. The total bioactive compound

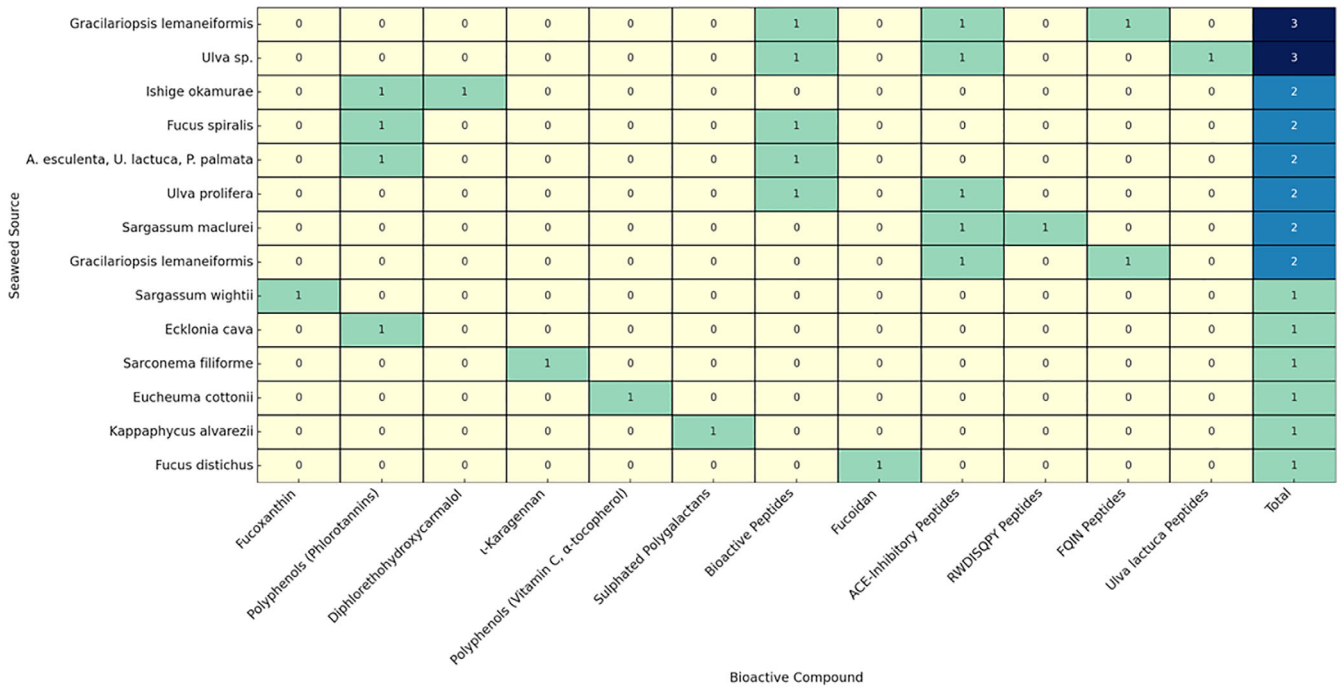


FIGURE 2 | Heatmap illustrating the distribution of bioactive compounds and peptides among different seaweed species. Original figure, created by the authors based on data compiled in this review; no third-party or copyrighted material was reproduced.

count of *G. lemaneiformis, A. esculenta, U. lactuca, P. palmata*, and *U. prolifera* demonstrates that these species possess greater biochemical diversity and show potential as antihypertensive sources. The species exhibit a high concentration of peptides that inhibit ACE activity and polyphenolic compounds, which have established connections to blood pressure control. The distribution of bioactive compounds shows distinct patterns among different species. The specific metabolites of a taxonomic group show different distribution patterns, as seen in fucoxanthin, which occurs mainly in brown algae like *S. wightii*, and ι-carrageenan, which appears in red algae such as *S. filiforme*. The specific distribution pattern of metabolites across species demonstrates how metabolite profiles that belong to particular species can affect their biological functions. The presence of ACE-inhibitory peptides and other bioactive peptides throughout both green and red algae species indicates that protein-derived substances have maintained their fundamental function to control the renin–angiotensin system [61, 92]. The various species display different combinations of compounds that they produce. The bioactive compounds of *F. spiralis* include phlorotannins, bioactive peptides, and ACE-inhibitory peptides, which create possibilities for different bioactive categories to interact with each other [57, 70].

The antihypertensive effects of seaweed derive from multiple metabolites that create different effects in the body according to this multicompound distribution. The study establishes three mechanisms, which include ACE inhibition, nitric oxide bioavailability enhancement, and antioxidant properties [60, 61, 64]. The heatmap shows that increased metabolite diversity results in better potential for antihypertensive effects. The study found that species with higher bioactive compound counts displayed multiple ways to affect health, which demonstrates that hypertension treatment needs to use multiple treatment methods. This finding provides a basis for prioritizing specific seaweed species for further investigation, particularly in the development of functional foods and nutraceutical applications.

3.6 | Mechanism of Action of Seaweed-Derived Bioactive Compounds and Peptides as Antihypertensive Agents

Hypertension stands as the most common cardiovascular disease, which serves as the primary cause of heart disease, stroke, and kidney damage [4, 93, 94]. The available pharmacological treatments show effectiveness in treating conditions; however, their extended use leads to harmful effects and patients developing dependency on medications [95, 96]. People now prefer safe and environmentally friendly solutions that come from natural sources such as seaweed bioactive compounds. This section shows experimental results about seaweed bioactive compounds and peptides that function as antihypertensive agents through their effects shown in Table 5.

The established patterns are validated through mechanistic proof, which shows how bioactive compounds decrease blood pressure through their effects on both molecular and physiological processes [24, 61]. *Sargassum wightii* contains fucoxanthin which functions as two separate treatments by blocking ACE and decreasing oxidative damage resulting in both lower vascular resistance and blood pressure drops [60]. *Fucus spiralis* shows phenolic compounds which inhibit ACE while *K. alvarezii* extracts sulfated polysaccharides show the same ability [68, 70]. The endothelial system uses DPHC, which comes from *I. okamurae*, to activate the PI3K/Akt/eNOS pathway that increases nitric oxide (NO) production for blood vessel widening [63].

TABLE 5 | Bioactive compounds and peptides derived from various seaweed species with reported antihypertensive mechanisms.

Bioactive compound	Source	Description	Mechanism	Reference
Polysaccharides and peptides	*A. esculenta, U. lactuca, P. palmata*	Seaweed polysaccharides and peptides that inhibit ACE-1.	Inhibit ACE-1, modulate enzyme activity by blocking active sites.	[57]
ACE-inhibitory peptides (KAF)	*U. prolifera*	Peptides that inhibit ACE and reduce blood pressure.	Inhibit ACE, increase NO production, and modulate calcium signaling pathways.	[58]
Fucoxanthin	*S. wightii*	Fucoxanthin is a pigment in brown algae with antioxidant, anti-inflammatory, and antihypertensive effects.	Decreases ACE activity, reduces hyperglycemia, prevents oxidative stress, and protects tissue morphology.	[61]
ACE-inhibitory peptides	*G. lemaneiformis*	Identified peptides with ACE-inhibitory potential for hypertension management.	Bind to the ACE active site, reducing its activity and angiotensin II production.	[61]
Polyphenols (Phlorotannins)	*E. cava*	Phlorotannins are bioactive polyphenolic compounds that have antioxidant properties.	Increases NRF2 and SOD2, reduces mtROS, and enhances mitochondrial biogenesis.	[62]
DPHC	*I. okamurae*	A polyphenolic compound with vasodilatory effects through calcium signaling.	Activates the PI3K/Akt/eNOS pathway, increases calcium levels in endothelial cells, and promotes NO production.	[63]
RWDISQPY peptides	*S. macclurei*	Peptides with ACE inhibitory effects.	Inhibit ACE, reduce endothelin-1 production, and lower blood pressure.	[64]
ι-Karagennan	*S. filiforme*	A sulfonated polysaccharide that works as a prebiotic.	Reduces systemic inflammation and modulates gut microbiota to lower blood pressure.	[65]
U. lactuca peptides	*Ulva* sp.	Peptides that exhibit ACE inhibitory activity.	Inhibit ACE-I, reduce angiotensin II production, and improve vascular function.	[67]
Sulfated polygalactans	*K. alvarezii*	Bioactive polysaccharides that inhibit ACE.	Inhibits ACE activity and reduces angiotensin II production.	[68]
FQIN-peptides	*G. lemaneiformis*	Peptides with significant ACE-inhibitory activity.	Inhibit ACE by noncompetitively binding to the active site and reducing ACE efficiency.	[69]
Bioactive peptides	*F. spiralis*	Peptides derived from enzymatic hydrolysis of proteins that inhibit ACE.	Inhibit ACE activity, reduce oxidative stress, and lower blood pressure.	[70]
Polyphenols (vitamin C, α-tocopherol)	*K. cottonii* (formerly *Eucheuma cottonii*)	Contains antioxidants that reduce oxidative stress.	Increases antioxidant enzyme activity (SOD, GPx) and reduces MDA levels.	[71]
Fucoidan	*F. distichus*	A bioactive compound known for anti-inflammatory and antihypertensive effects.	Activates SIRT6, reduces inflammation, and prevents oxidative stress.	[72]

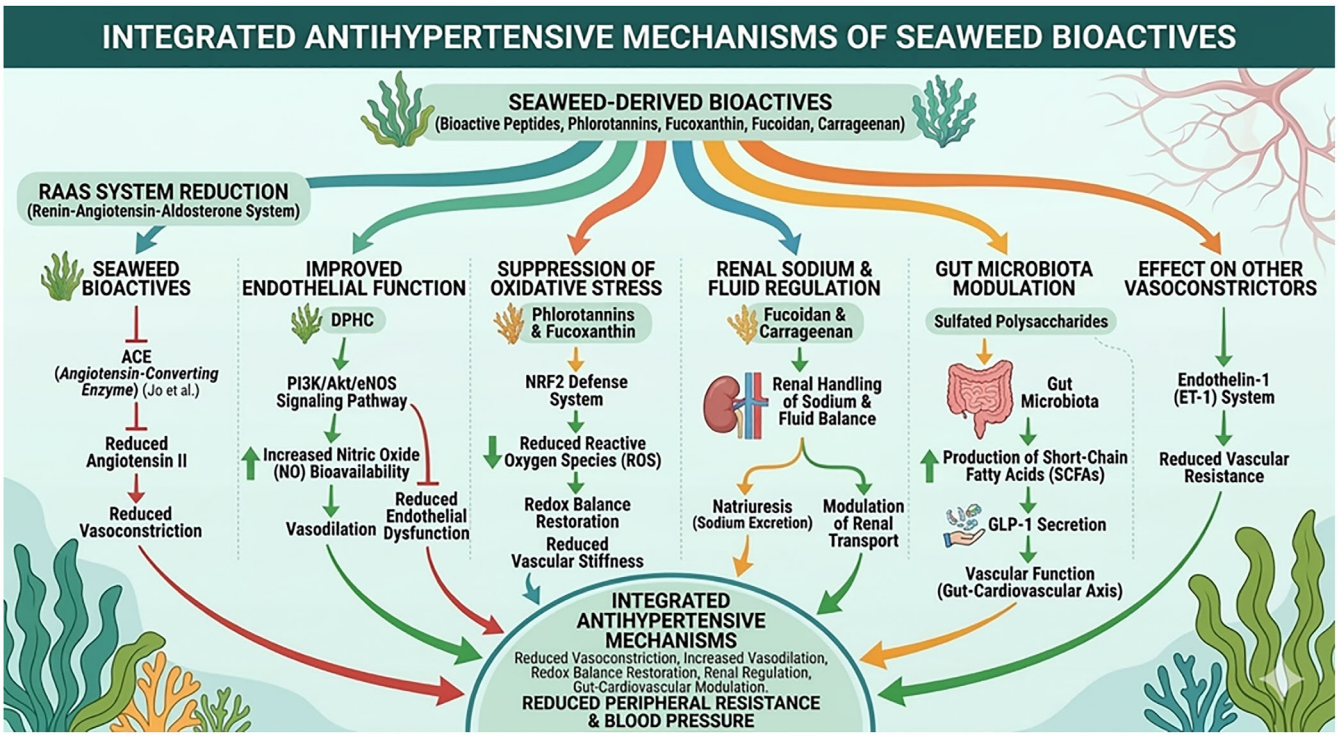


FIGURE 3 | Integrated antihypertensive mechanisms of seaweed-derived bioactive compounds. Original figure, created by the authors; no third-party or copyrighted material was reproduced.

The mechanism establishes its essential function for restoring endothelial function, which gets disrupted during hypertensive episodes [97]. The development of hypertension results from oxidative stress, which acts as a primary factor in the disease. The phlorotannin dieckol from *E. cava* functions as an antioxidant booster because it activates three pathways, which protect cells from ROS and help maintain healthy blood vessel function [1, 62]. The polysaccharides carrageenan and fucoidan show vascular effects, which extend to their capability of reducing inflammation and changing gut bacteria and their potential role in controlling sodium levels in kidneys [49, 65, 79].

Blood pressure control is enhanced through the application of bioactive peptides that originate from seaweed. The peptides KAF from *U. prolifera* and SFYYGK and RLVPVPY from *G. lemaneiformis* and VA and CL from *V. aegagrophila* and *C. linum* demonstrate strong inhibition of ACE activity [59, 61, 92]. Some peptides show the ability to perform multiple functions through their biological effects. The peptide RWDISQPY from *S. macclurei* not only inhibits ACE but also reduces ET-1, a potent vasoconstrictor, highlighting the multi-target nature of seaweed-derived antihypertensive agents [64].

3.7 | Integrated Antihypertensive Mechanism of Seaweed Bioactives

As illustrated in Figure 3, seaweed-derived bioactive compounds exert antihypertensive effects through interconnected and multi-target mechanisms. Based on the experimental findings discussed in the previous section, seaweed-derived bioactives can be understood within an integrated antihypertensive framework. Hypertension is a multifactorial disorder involving complex interactions among vascular, renal, neural, and endocrine systems. Seaweed bioactives exert antihypertensive effects through coordinated modulation of multiple physiological pathways rather than a single molecular target [25, 98]. A central mechanism involves inhibition of the RAAS, where bioactive compounds reduce angiotensin II formation and downstream vasoconstriction [24]. This is closely linked with improvements in endothelial function through enhanced nitric oxide (NO) bioavailability via activation of PI3K/Akt/eNOS signaling pathways [63]. These effects are further reinforced by suppression of oxidative stress. By reducing ROS and activating antioxidant pathways such as NRF2, seaweed bioactives help restore endothelial integrity and vascular function [62, 75].

Beyond vascular mechanisms, additional pathways contribute to blood pressure regulation. Seaweed polysaccharides may influence renal sodium handling and fluid balance, which are key determinants of long-term blood pressure control [49, 37]. Furthermore, modulation of gut microbiota and increased production of SCFAs can enhance metabolic and vascular regulation through the gut–cardiovascular axis [79]. In addition, certain bioactive peptides may reduce ET-1, thereby attenuating vasoconstriction and further lowering vascular resistance [64]. Overall, these mechanisms are highly interconnected. The combined effects of RAAS inhibition, endothelial restoration, oxidative stress suppression, renal regulation, and gut microbiota modulation lead to improved vascular homeostasis, reduced peripheral resistance, and ultimately blood pressure reduction. This integrative multitarget mechanism highlights the potential of seaweed-derived bioactives as promising candidates for functional antihypertensive interventions.

4 | Conclusion

This review indicates that seaweed-derived bioactive compounds and peptides show promising antihypertensive potential through integrated multitarget mechanisms, including modulation of the RAAS, enhancement of endothelial nitric oxide signaling, suppression of oxidative stress, and regulation of inflammatory pathways. Evidence from in vitro and in vivo studies is broadly consistent with a role in blood pressure reduction, with compounds such as fucoxanthin, phlorotannins, diphlorethohydroxycarmalol, and sulfated polysaccharides appearing to act through complementary mechanisms; however, most of this evidence still derives from single studies per species, so these findings should be interpreted as preliminary rather than conclusive.

However, the current evidence is largely limited to preclinical studies and a single database source, which may restrict generalizability. Future research should prioritize well-designed clinical trials, dose optimization, and comparative studies across seaweed species. Overall, seaweed-derived bioactives represent promising candidates for the development of functional foods and nutraceutical interventions for hypertension management. These findings provide a scientific basis for the development of next-generation functional foods and marine-derived nutraceuticals targeting hypertension.

Author Contribution

F.M.: conceptualization, methodology, investigation, data curation, formal analysis, writing – original draft. M.F.: supervision, methodology, validation, writing – review and editing. D.S.: supervision, validation, data curation, writing – review and editing. M.R.: supervision, conceptualization, writing – review and editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Use of Generative AI and AI-Assisted Technologies in the Writing Process

The authors used AI-assisted tools solely to improve the language, grammar, clarity, and readability of the article. The authors carefully reviewed and edited all AI-assisted suggestions and take full responsibility for the accuracy, originality, scientific content, interpretation of the data, and conclusions presented in this work.

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