IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
onal Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 3, July 2026
Impact Factor: 8.2

Marine-Derived Bioactive Compounds as Neuroprotective Candidates: Mechanisms, Screening Models and Quality-Control Considerations

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Abstract: *Marine-derived bioactive compounds have attracted attention in neuropharmacology because algae, seaweeds and marine microorganisms produce chemically diverse metabolites with antioxidant, anti-inflammatory, pigment-related and polysaccharide-related activities. Neurodegenerative disorders are mechanistically complex and involve oxidative stress, neuroinflammation, mitochondrial dysfunction, cholinergic impairment, apoptosis and abnormal protein handling. This review summarizes the scientific rationale for studying fucoxanthin, astaxanthin, phlorotannins and sulfated polysaccharides as candidate neuroprotective agents. It also discusses in vitro assays, neuronal cell-line models, scopolamine-induced cognitive impairment, behavioural tests, biochemical markers, cytokines, histopathology and quality-by-design controls. The review emphasizes conservative interpretation: antioxidant activity in a chemical assay is supportive but not sufficient to establish neuroprotection, and a positive animal result cannot be translated directly into clinical efficacy. A staged screening framework is proposed in which source authentication, chemical standardization, non-toxic concentration selection, behavioural outcomes and mechanistic markers are integrated. Marine natural products may provide useful leads for future neuroprotective research, but their development requires reproducible sourcing, marker confirmation, pharmacokinetic evaluation, brain exposure studies, chronic disease models and regulatory toxicology.*

Keywords: Marine bioactives; fucoxanthin; astaxanthin; phlorotannins; fucoidan; neurodegeneration; oxidative stress; scopolamine model

I. INTRODUCTION

Neurodegenerative disorders constitute a growing public health concern because they produce progressive impairment in memory, movement, behaviour and independence. The underlying biology is not limited to neuronal death alone; it involves disturbed synaptic communication, oxidative injury, mitochondrial stress, chronic inflammatory activation and

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failure of compensatory repair systems [1-4]. This complexity creates a need for discovery strategies that examine more than one target and more than one experimental endpoint.

Marine biodiversity is an important source of chemically distinctive natural products. Algae and seaweeds are exposed to salinity, ultraviolet radiation, variable oxygen tension and ecological competition. These environmental pressures support the formation of carotenoids, phenolics, sulfated polymers and other metabolites with possible biological activity [5,27-30]. Marine-derived materials are therefore relevant to neuroprotective screening, particularly when the screening question is framed as preclinical lead identification rather than direct clinical treatment.

This review presents a structured and original academic synthesis of marine-derived compounds in neuroprotection. It focuses on mechanism, compound classes, assay selection and interpretation standards. The review also highlights the need for quality-by-design controls because natural product variability can otherwise weaken experimental conclusions.

Review approach

The review was organized as a narrative literature synthesis. Sources were selected around neurodegenerative mechanisms, marine bioactive compounds, antioxidant and cholinergic assays, cell-line cytoprotection, scopolamine-induced cognitive impairment, behavioural pharmacology, biochemical markers and histopathological confirmation. Priority was given to peer-reviewed articles, recognized guideline documents and methodological publications that support experimental design. The review does not attempt a quantitative meta-analysis because the available literature differs widely in source material, extraction method, model system, dose and endpoint selection.

Mechanistic basis of neuroprotection

Oxidative stress

Oxidative stress is central to many neurodegenerative mechanisms. Neuronal membranes contain abundant lipids, and the brain has high oxygen demand. Excess reactive species can trigger lipid peroxidation, protein oxidation and mitochondrial injury. Malondialdehyde is commonly used as an index of lipid peroxidation, while glutathione, superoxide dismutase and catalase represent endogenous antioxidant defence [19-24]. A material showing reduced MDA with restoration of GSH, SOD and catalase provides stronger mechanistic evidence than a material showing only chemical radical scavenging.

Neuroinflammation

Activated glial cells and inflammatory mediators may amplify neuronal damage. Cytokines such as TNF-alpha, IL-1beta and IL-6 can disturb synaptic function and contribute to progressive injury. Marine compounds with anti-inflammatory potential require confirmation in biological systems because suppression of a single inflammatory marker is not sufficient to claim disease modification [4,10-12].

Cholinergic impairment

The cholinergic system contributes to attention and memory. Acetylcholinesterase degrades acetylcholine, and excessive acetylcholinesterase activity may reduce synaptic acetylcholine availability. Donepezil and related drugs provide a comparator in cognition-related models. In vitro AChE inhibition by marine compounds is mechanistically interesting, but it must be linked with brain AChE levels and behavioural recovery before a neuroprotective interpretation is made [15,19].

Mitochondrial and apoptotic pathways

Mitochondrial dysfunction reduces ATP availability, increases oxidative stress and can trigger apoptotic signalling. Carotenoids and polyphenols are often examined for their ability to preserve mitochondrial integrity, but such effects require cell-based or tissue-based confirmation rather than inference from chemical structure alone.

Major marine-derived compound classes

Fucoxanthin and fucoxanthinol

Fucoxanthin is a brown algal xanthophyll carotenoid characterized by an allenic bond, epoxide group and conjugated polyene chain. Its proposed relevance includes antioxidant, anti-inflammatory and mitochondrial support.

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Fucoxanthinol, a metabolite of fucoxanthin, is important in bioavailability discussions. Poor water solubility, light sensitivity and lipid-dependent absorption are practical limitations for experimental use [6,7,13].

Astaxanthin

Astaxanthin is a xanthophyll carotenoid found in microalgae and marine animals. It is widely discussed as a membrane-associated antioxidant. Its lipophilicity can be an advantage for membrane protection but a limitation for aqueous dosing systems. Experimental design should therefore document dispersion, vehicle compatibility and storage conditions [8,9].

Phlorotannins

Phlorotannins such as eckol and dieckol are brown-algal polyphenols derived from phloroglucinol units. Their hydrogen-bonding capacity, radical-scavenging potential and enzyme modulation make them relevant to neuroprotective screening. Their molecular size, polarity and matrix composition influence absorption and biological availability [10,12,14].

Sulfated polysaccharides and fucoidan-like fractions

Sulfated polysaccharides are heterogeneous marine polymers with potential anti-inflammatory and immunomodulatory properties. Their biological response depends on molecular weight, sulfate content, monosaccharide composition and extraction process. Because composition varies by source and method, marker-based standardization is essential [11,28,29].

Experimental screening models

Chemical antioxidant assays such as DPPH, ABTS, FRAP and nitric oxide scavenging are useful for early ranking of activity. They are inexpensive and reproducible when carefully controlled, but they do not represent metabolism, blood-brain barrier access or tissue distribution. Therefore, chemical assays should be treated as screening tools rather than proof of neuroprotection.

Cell-line models such as SH-SY5Y or PC12 cells provide a bridge between chemical assays and animal studies. They can identify non-toxic concentrations and test protection against induced oxidative or neurotoxic injury. Interpretation must distinguish basal cytotoxicity from true cytoprotection. A non-toxic compound may still be biologically inactive, while a compound with apparent protection may be unsuitable if it shows basal toxicity.

Scopolamine-induced cognitive impairment is widely used as an acute pharmacological model related to cholinergic dysfunction. It is useful for preliminary memory screening but should not be treated as a complete model of Alzheimer disease or chronic neurodegeneration. Morris water maze, Y-maze and novel object recognition provide complementary evidence of spatial memory, working memory and recognition memory [15-18].

Quality-by-design in marine neuroprotective screening

Quality-by-design is particularly valuable in natural product research because source variation can strongly influence chemical content and biological response. A quality target profile should define a traceable marine source, reproducible marker content, acceptable solubility or dispersion, non-toxic concentration range and compatibility with selected assays. Critical material attributes include species identity, collection site, season, drying method, particle size and solvent system. Critical process parameters include extraction ratio, extraction time, temperature, filtration, concentration, drying and storage.

Risk assessment should rank uncertain authentication, variable marker content, light-sensitive carotenoids, poor solubility, cytotoxic concentration and vehicle incompatibility as high-priority risks. Use of a single standardized batch for in vivo studies improves interpretability. Without these controls, a positive or negative result may reflect material variation rather than true pharmacological activity.

Endpoint integration and interpretation

Neuroprotection is a multi-level concept. Behavioural improvement indicates functional relevance, but it can be confounded by sedation, stimulation, anxiety or motor impairment. Biochemical markers provide mechanistic support, but they do not confirm tissue preservation by themselves. Histopathology supplies morphological confirmation when it demonstrates preserved hippocampal architecture and reduced degenerative features.

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The strongest interpretation arises when behavioural, biochemical, inflammatory and histological findings move in the same protective direction. Partial findings should be described with partial language. For example, an extract that shows antioxidant activity but does not improve behaviour should be described as an antioxidant candidate requiring further confirmation. A sample that improves behaviour and reduces oxidative stress but does not affect cytokines may be described as showing partial oxidative pathway-linked protection.

Translational limitations and future directions

Several barriers limit direct translation of marine neuroprotective candidates. These include poor aqueous solubility, uncertain oral absorption, limited brain exposure, polymer heterogeneity, incomplete toxicity information and differences between acute models and human chronic disease. Future research should include LC-MS or HPLC marker profiling, pharmacokinetic and brain distribution studies, repeated-dose toxicity, chronic neurodegeneration models and molecular confirmation of pathways such as Nrf2, NF-kB, BDNF and apoptosis markers.

Formulation development may be needed for lipophilic carotenoids or high-molecular-weight polysaccharides. Nanocarriers, lipid systems or standardized extracts may improve dispersion, stability and exposure, but formulation changes must be evaluated separately because they can alter both efficacy and safety.

II. CONCLUSION

Marine-derived bioactive compounds provide a scientifically promising but experimentally demanding area for neuroprotective research. Fucoxanthin, astaxanthin, phlorotannins and sulfated polysaccharides can be rationally studied because they align with oxidative, inflammatory and cholinergic mechanisms. However, neuroprotective claims require staged validation, quality-controlled material, non-toxic concentration selection, behavioural evidence, biochemical support and histopathological confirmation. The future of this field depends on conservative interpretation, reproducible methods and careful movement from preclinical screening toward translational evaluation.

Table 1. Marine classes and neuroprotective relevance

Class	Representative examples	Key relevance	Main limitation
Carotenoids	Fucoxanthin, fucoxanthinol, astaxanthin	Antioxidant and membrane-related protection	Poor water solubility and light sensitivity
Phlorotannins	Eckol, dieckol	Polyphenolic antioxidant and enzyme modulation	Variable absorption and matrix effects
Sulfated polysaccharides	Fucoidan-like fractions	Anti-inflammatory and immunomodulatory relevance	Polymer heterogeneity and molecular weight variation
Marine peptides	Bioactive peptides	Possible antioxidant and signalling effects	Source and sequence variability

Table 2. Screening methods and interpretation limits

Method	Useful output	Interpretation limit
DPPH/ABTS/FRAP/NO assays	Chemical antioxidant profile	Does not prove brain activity
AChE assay	Cholinergic enzyme inhibition	Must be linked to behavioural and brain AChE data
MTT/resazurin cell assay	Non-toxic range and cytoprotection	Cell culture does not reproduce whole-body pharmacokinetics
Scopolamine model	Cognition-related behavioural change	Acute model; not a full chronic neurodegeneration model
Histopathology	Tissue preservation	Requires standardized scoring and blinded assessment

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Table 3. Future research priorities

Priority	Recommended method	Purpose
Marker confirmation	HPLC/LC-MS	Chemical identity and batch comparison
Brain exposure	Pharmacokinetic and tissue distribution study	Confirm delivery to target tissue
Mechanistic proof	ELISA, Western blot, gene expression	Validate pathways such as Nrf2/NF-kB/BDNF
Safety	Repeated-dose toxicity	Translational readiness
Formulation	Lipid or nanocarrier systems	Improve solubility and stability when justified

Ethical statement

The manuscript is prepared as a preclinical protocol and reporting framework. Animal experimentation, if performed, should be conducted only after approval from the Institutional Animal Ethics Committee and in accordance with applicable national laboratory animal guidelines [25].

Conflict of interest

The authors should declare any financial or non-financial conflict of interest before journal submission.

Funding

Funding information should be inserted as applicable. If no funding was received, the authors may state: No external funding was received.

REFERENCES

1. Aebi H. Catalase in vitro. Methods Enzymol. 1984;105:121-126.
2. Ambati RR, Phang SM, Ravi S, Aswathanarayana RG. Astaxanthin: sources, extraction, stability, biological activities and commercial applications. Mar Drugs. 2014;12(1):128-152.
3. Beauchamp C, Fridovich I. Superoxide dismutase: improved assays and an assay applicable to acrylamide gels. Anal Biochem. 1971;44(1):276-287.
4. Bradford MM. A rapid and sensitive method for quantitation of microgram quantities of protein using the principle of protein-dye binding. Anal Biochem. 1976;72:248-254.
5. Cummings J, Lee G, Nahed P, Kambar MEZN, Zhong K, Fonseca J, Taghva K. Alzheimer's disease drug development pipeline: 2023. Alzheimers Dement. 2023;9(2):e12385.
6. Dhamale GR, Shinde PB, Rajguru JR. A Review: Gastroretentive Drug Delivery Systems. *International Journal of Pharmaceutical Sciences*. pp.1825–1840. doi:10.5281/zenodo.12818744.
7. D'Hooge R, De Deyn PP. Applications of the Morris water maze in the study of learning and memory. Brain Res Brain Res Rev. 2001;36(1):60-90.
8. Doke R, Rajguru J, Vinchurkar K. Personalized Medicine Through AI-Driven Imaging. In: *Springer Nature*. doi:10.1007/978-3-032-02963-8_7.
9. D'Orazio N, Gemello E, Gammone MA, de Girolamo M, Ficoneri C, Riccioni G. Fucoxanthin: a treasure from the sea. Mar Drugs. 2012;10(3):604-616.
10. Dugger BN, Dickson DW. Pathology of neurodegenerative diseases. Cold Spring Harb Perspect Biol. 2017;9(7):a028035.
11. Ellman GL, Courtney KD, Andres V Jr, Feather-Stone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem Pharmacol. 1961;7(2):88-95.

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12. Ennaceur A, Delacour J. A new one-trial test for neurobiological studies of memory in rats. Behav Brain Res. 1988;31(1):47-59.
13. Fitton JH. Therapies from fucoidan: multifunctional marine polymers. Mar Drugs. 2011;9(10):1731-1760.
14. Gade AC, et al. Virtual screening of a marine natural product database for in silico acetylcholinesterase inhibition. Mar Drugs. 2023;21(9):477.
15. Gawai NM, Jadhav RR, Modak A, Sawarkar HS, Rajguru JR. Advancements in Nanogel Technology for Drug Delivery: Current Innovations and Future Perspectives. *African Journal of Biomedical Research*. 2024;27(3S):3200–3212. doi:10.53555/AJBR.v27i3S.2905.
16. Gawari PB, Rajguru JR. Confronting the Nipah Virus: Critical Insights and Practical Recommendations. *International Journal of Creative Research Thoughts (IJCRT)*. 2026;14(2). ISSN: 2320-2882.
17. Higuera-Ciapara I, Felix-Valenzuela L, Goycoolea FM. Astaxanthin: a review of its chemistry and applications. Crit Rev Food Sci Nutr. 2006;46(2):185-196.
18. Ingole RD, Gawai NM, Rajguru JR. Nanoformulation of Vitamin D Derivatives and Metabolites. *African Journal of Biomedical Research*. 2024;27(4S). doi:10.53555/AJBR.v27i4S.4897.
19. Kim SK, Wijesekara I. Development and biological activities of marine-derived bioactive peptides: a review. J Funct Foods. 2010;2(1):1-9.
20. Klinkenberg I, Blokland A. The validity of scopolamine as a pharmacological model for cognitive impairment: a review. Neurosci Biobehav Rev. 2010;34(8):1307-1350.
21. Kushwah P, Rajguru JR, Jain G, Patidar A, Tomar PS. A Review of Classic Cures for Contemporary Marvels: Unveiling the Medicinal Secrets of *Piper betle* Linn. Leaves and *Nyctanthesarbor-tristis*. *International Journal of Creative Research Thoughts (IJCRT)*. 2024;12(1)–D747.
22. Kwon YJ, Jung H, Kim MJ, Kim J. Therapeutic effects of phlorotannins in neurodegenerative disease: antioxidant, anti-inflammatory and enzyme-modulating actions. Front Mol Neurosci. 2023;16:1181016.
23. Lomartire S, Marques JC, Goncalves AMM. Marine macroalgae polyphenols as potential neuroprotective antioxidants in neurodegenerative diseases. Mar Drugs. 2023;21(5):270.
24. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem. 1951;193(1):265-275.
25. Morris R. Developments of a water-maze procedure for studying spatial learning in the rat. J Neurosci Methods. 1984;11(1):47-60.
26. Newman DJ, Cragg GM. Natural products as sources of new drugs over nearly four decades. J Nat Prod. 2020;83(3):770-803.
27. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem. 1979;95(2):351-358.
28. Organisation for Economic Co-operation and Development. Test No. 423: Acute Oral Toxicity - Acute Toxic Class Method. Paris: OECD Publishing; 2002.
29. Pangestuti R, Kim SK. Neuroprotective effects of marine algae. Mar Drugs. 2011;9(5):803-818.
30. Peng J, Yuan JP, Wu CF, Wang JH. Fucoxanthin, a marine carotenoid present in brown seaweeds and diatoms: metabolism and bioactivities relevant to human health. Mar Drugs. 2011;9(10):1806-1828.
31. Pruccoli L, et al. Antioxidant and neuroprotective effects of fucoxanthin and fucoxanthinol: comparative preclinical considerations. Curr Issues Mol Biol. 2024;46(2):1128-1147.
32. Rajguru JR, Gawari PB, Desai RS, Isal AA. Overview of Intrauterine Drug Delivery System. *International Journal of Creative Research Thoughts (IJCRT)*. 2024;12(1)–D316.
33. Rajguru JR, Navghare AB, Shinde SP, Pawar PP, Lokhande PB. An Overview of Implantable Drug Delivery Systems. *International Journal of Creative Research Thoughts (IJCRT)*. 2024;12(1)–F958.
34. Rajguru JR, Shinde PB, Shinde SP, Humbe KA, Pawar PP. Nasal Routes of Drug Delivery: A Creative Approach. *International Journal of Creative Research Thoughts (IJCRT)*. 2024;12(1)–E477.

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35. Sitaphale GR, Tathe PR, Laddha PR, Charhate KB, Rajguru JR. Phytochemical Screening, Isolation, and Characterization of Extract from Various Parts of *Phoenix sylvestris*. *African Journal of Biomedical Research*. 2024;27(3S):3368–3374. doi:10.53555/AJBR.v27i3S.2938.
36. Tathe PR, Laddha PR, Sitaphale GR, Charhate KB, Pimple UA, Jadhao YD, Alhat RM, Rajguru JR. Studies in Preparation and Evaluation of Nanoparticles for Controlled Drug Delivery of Peptide-Based Drugs. *African Journal of Biomedical Research*. 2024;27(3S):3179–3190. doi:10.53555/AJBR.v27i3S.2894.
37. Wayal SR, Barke SA, Darekar SM, Jalindar AS, Gawai NM, Wankhede HR, Bathe RS, Rajguru JR. Development of Currant-Loaded Nanoparticles and Phytosomes for Enhanced Antioxidant Delivery. *International Journal of Environmental Sciences*. 2025;11(22S):4067–4071. doi:10.64252/p2tecx31.
38. Wayal SR, Darekar SM, Jalindar AS, Motr PR, Gawai NM, Bodake PL, Barke SA, Dongare AB, Rajguru JR. Development of a Validated HPTLC Method for the Simultaneous Estimation of Curcumin and Berberine in DashamoolaKvatha. *International Journal of Environmental Sciences*. doi:10.64252/kq9rtn45.
39. Wayal SR, Rajguru JR, Bhise MR. A Systematic Review on the Effective Teaching Strategies and Methods for Cancer Patient Education. *Journal of Cancer Education*. 2025. doi:10.1007/s13187-025-02759-z.
40. Wijesinghe WAJP, Jeon YJ. Biological activities and potential industrial applications of fucose-rich sulfated polysaccharides and fucoidans isolated from brown seaweeds: a review. Carbohydr Polym. 2012;88(1):13-20.
41. Wilson DM, Cookson MR, Van Den Bosch L, Zetterberg H, Holtzman DM, Dewachter I. Hallmarks of neurodegenerative diseases. Cell. 2023;186(4):693-714.
42. World Health Organization. Dementia. Geneva: WHO; 2025.
43. World Health Organization. Parkinson disease. Geneva: WHO; 2023.
44. Zhu L, Chen X, Liu X, Wang L. Marine-derived polysaccharides: potential agents against neurodegenerative diseases. Front Pharmacol. 2024;15:1346298.