Designing brain-boosting functional foods:
Using Galician macroalgae for smart nutrition

P. Barciela [1]; A. Perez-Vazquez [1]; M. Carpena [1]; A.O.S. Jorge [1, 2]; E. Yuksek; A. Silva [1, 3]; M.A. Prieto [*, 1]

[1] Instituto de Agroecoloxía e Alimentación (IAA), Universidade de Vigo, Nutrition and Food Group (NuFoG), Campus Auga, 32004 Ourense, Spain.

[2] REQUIMTE/LAQV, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, R. Jorge Viterbo Ferreira 228, 4050-313 Porto, Portugal

[3] REQUIMTE/LAQV, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr António Bernardino de Almeida 431, 4200-072 Porto, Portugal.

1 INTRODUCTION

Marine macroalgae are emerging as a **high value functional category** owing to their **biochemical composition, low environmental footprint,** and **biotechnological versatility.** The **Galician coast** is home to several species of seaweed, including **brown algae** such as *Fucus vesiculosus* and *Saccharina latissima* ("sugar kelp") and **red algae** such as *Palmaria palmata,* which have been found to be suitable for **industrial applications. Nootropics**, also labelled as **smart drugs**, are substances formulated over several decades initially intended to **treat** specific **brain imbalances. Macroalgae** can concentrate **bioactive compounds (BCs)** of nootropic interest, such as **polyphenols, polysaccharides, omega-3 fatty acids,** and **amino acids.** These **BCs** have **anti-amyloidosis, anticholinesterase, antioxidant, anti-inflammatory,** and **neuroprotective** effects, supporting their potential as **functional foods.** Notably, studies reveal that dietary interventions can **lower** the risk of **neurodegenerative** diseases, such as **dementia**, by **30-50% with adherence.**

2 METHODOLOGY

This review was carried out using the **ScienceDirect** and **PubMed** databases to compile articles from **Q1** journals between **2020** and **2025.** The inclusion criteria were based on keywords including **"functional foods," "Macroalgae," "nootropics,"** and **"bioactive compounds".** Data screening and extraction were conducted in accordance with **PRISMA guidelines.**

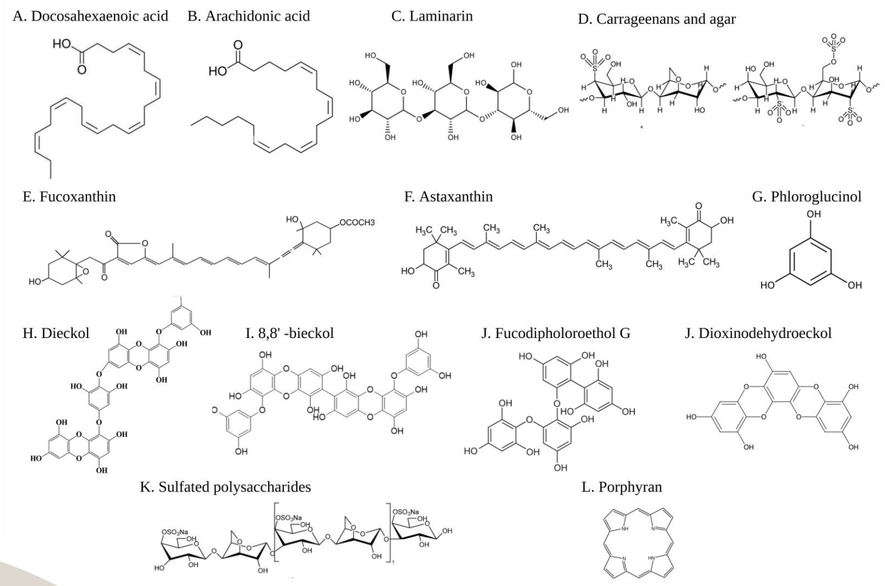

Figure 1: Structural formulas of biologically active compounds from brown and red macroalgae with neuroenhancing effects.

3 OBJECTIVE

Identify **bioactive compounds** linked to **mechanisms** that enhance **neuroplasticity**, **synaptogenesis**, and **the modulation of oxidative stress in the brain.**

4 RESULTS

Major cognitive enhancer BCs extracted from **macroalgae** primarily include omega-3 fatty acids (docosahexaenoic acid, arachidonic acid), sulfated polysaccharides (**fucoidan, laminarin, porphyran**), phlorotannins (**dieckol, 8,8'-bieckol, fucodiphloroethol G, dioxinodehydroeckol, phloroglucinol**), and carotenoids (**fucoxanthin, astaxanthin**), as well as polysaccharides from **red algae** (**carrageenans, agar**) **(Figure 1).**

The effects of **these nutrients** are achieved through multiple mechanisms. **Antioxidant activity** can **restore redox balance and prevent oxidative/ nitrosative stress.** Targeting inflammatory immune modulation and gut microbiota regulation offers promising avenues for mitigating **neuroinflammation**. **Augmenting neurotrophic factor (NTF)** fosters neural cell **maturation, proliferation,** and **survival.** Additionally, certain compounds promote **brain health, recall, and cognitive function** by modulating **neurotransmitter synthesis** and **storage** for **fast release**.

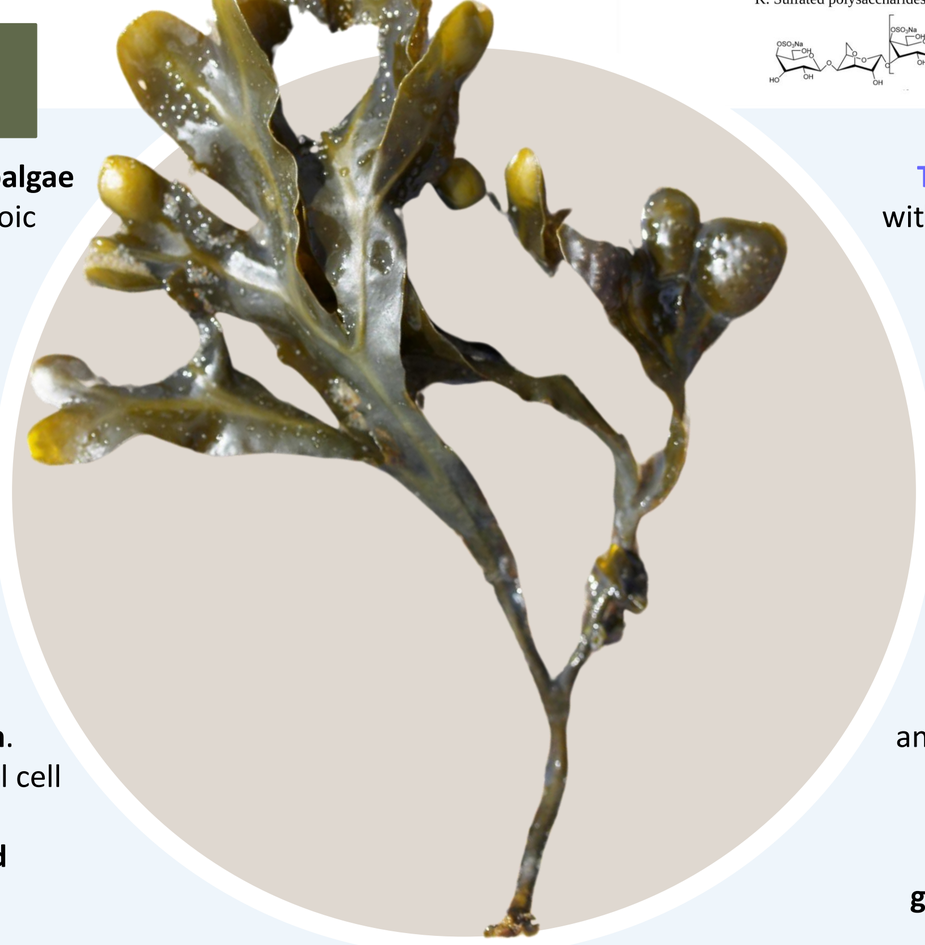

Table 1 summarizes studies on **BCs** from **macroalgae** with confirmed **nootropic and neuroprotective** effects. **Available real-world products** include ***E3Live®***, a spirulina-based beverage from blue-green algae harvested from **Klamath Lake**. ***E3Live®*** is rich in nutrients and antioxidants that support **energy metabolism**, **mental clarity**, and **wellness**. ***BrainON®*** is an all-natural supplement designed to **optimize brain function** and **unlock mental potential.** Its formula is made from fresh-frozen ***Aphanizomenon flos-aquae*** **(AFA)** and combines extracts of **phenylethylamine** and **phycocyanin**. Finally, ***Algalithe® Brain+,*** is a product based on *Lithothamnion*, a **red algae** that absorbs calcium, and magnesium from its environment. It is formulated to **boost brain health** and **support gut health.** ***Algalithe® Brain+*** is sold as tablets, capsules, and powder sachets. **Clinical trials** show support for the **gut–brain axis, intestinal barrier integrity,** and **stress resilience.**

Table 1. Cognitive-enhancing macroalgae BCs: mechanism of action, cytotoxicity, methodology, and effective dosage.

Species	Comp. / sample	Purity	Mechanism of action	Cytotoxicity / neuroprotection	Experimental model / endpoint	Effective dose / conc.	Conf. act.	Ref.
F. vesiculosus **(B)**	Fucoidan (low MW)	High	Aa, anti-apoptotic, prevents dopaminergic neuron loss	>98% cell viability at 100 µg/mL, non- cytotoxicity	***In vitro***: PC-12 cells; MTT, ThT, TEM, Hoechst staining	~50 mg/kg in rat	✓	Alghazwi et al., 2019
P. tenera **(R)**	Sulfated galactans, MAAs	High	Aa, anti-inflammatory, ↓Aβ & tau, restores gut microbiota and TJ proteins	Neuroprotective effect against $PM_{2.5}$-induced cognitive ↓	***In vivo***: mouse model exposed to $PM_{2.5}$; Y-maze, MWM, mitochondrial assays, TJ protein and SCFA analyses	200 mg/kg (oral)	✓	Kyeong Park et al., 2022
H. elongata **(B)**	SG	Crude	LXRs and PPARs activation, ↑cholesterol efflux genes, ↓ FA synthesis genes	Non-cyt. (lipid metabolism modulation)	***In vitro***: LXR/PPAR reporter assays, lipidomic profiling	Dose adjusted based on SG content	✓	Martens et al., 2023
S. polycystum **(B)**	Gallic acid	Crude	Strong Aa (↑SOD, CAT, GSH-Px; ↓MDA); inhibition of S100B protein; ROS scavenging; modulation of HBO	↑cognitive performance, non- cytotoxicity	***In vivo***: rat model of ischemic stroke (MCAO); MWM and NOR tests	100, 300, 500 mg/kg BW (oral, 35 days)	✓	Khongrum et al., 2024
E. cava **(B)**	Dieckol	>95%	↑ of the Nrf2/HO-1 antioxidant pathway, ATP depletion, loss of $\Delta\Psi m$, and Ca^{2+} and ROS overload	Non- cytotoxicity below 100 µM	***In vitro:*** Primary cortical neurons and HT22 cells exposed to glutamate (100 µM, 24 h; 5 mM, 12 h)	1–50 µM (pretreatment 1 h before glutamate)	✓	Cui et al., 2019

Abbreviations: *Fucus vesiculosus*; **Aa**: Antioxidant activity; **MW**: Molecular weight; **PC-12**: Pheochromocytoma-12 cells; **MTT**: 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay; **ThT**: Thioflavin T; **TEM**: Transmission electron microscopy; **Hoechst**: Hoechst 33258 nuclear stain; *P. tenera*: *Porphyra tenera*; **MAAs**: Mycosporine-like amino acids; **TJ**: Tight junction proteins; **SCFAs**: Short-chain fatty acids; **MWM**: Morris water maze; *H. elongata*: *Himanthalia elongata*; **LXRs**: Liver X receptors; **PPARs**: Peroxisome proliferator-activated receptors; **FA**: Fatty acids; **SG**: Sulfated galactans; *S. polycystum*: *Sargassum polycystum*; **NOR**: Novel object recognition; **HBO**: Hippocampal oxidative balance; **ROS**: Reactive oxygen species; **HO-1**: Heme oxygenase-1; **Nrf2**: Nuclear factor erythroid 2–related factor 2; **ATP**: Adenosine triphosphate; **(B)**: Brown alga; **(R)**: Red alga.

5 CONCLUSION

These findings suggest **macroalgae** may support **brain health and mental performance through diet when nutrition** and **neuroscience are combined.** Yet, **variability** in bioactive composition, inconsistent **standardization** and dosages, minimal **clinical evidence**, and the risk of **contamination** or reduced **bioavailability** in extracts raise concerns about the long-term **effectiveness** of this **functional line.**

ACKNOWLEDGMENTS

This research was supported by MICIU/AEI/10.13039/501100011033 through the predoctoral industrial grant for A. Pérez-Vázquez (DIN2024-013416), in collaboration with Mercantia Desarrollos Alimentarios, S.L., as well as by the Xunta de Galicia through the predoctoral grant for P. Barciela (ED481A-2024-230). The authors thank the National Funding by FCT (Foundation for Science and Technology) for the research grant awarded to A.O.S. Jorge (2023.00981.BD), which can be accessed via the DOI identifier: https://doi.org/10.54499/2023.00981.BD. This work also received financial support from Portuguese national funds (FCT/MECI, Fundação para a Ciência e a Tecnologia, and o Ministério da Educação, Ciência e Inovação) through the UID/50006 project, Laboratório Associado para a Química Verde - Tecnologias e Processos Limpos.