

Sea cucumber functional potential: meta-analysis of knowledge needs and trends

2nd HOLOSUSTAIN workshop

Ålesund 20th May 2022
Miroslava Atanassova – Møreforsking
Olafur Fridjonsson - Matis

Last published guide on Sea CUCUMBERS AS FOOD SOURCE by FAO from 2012

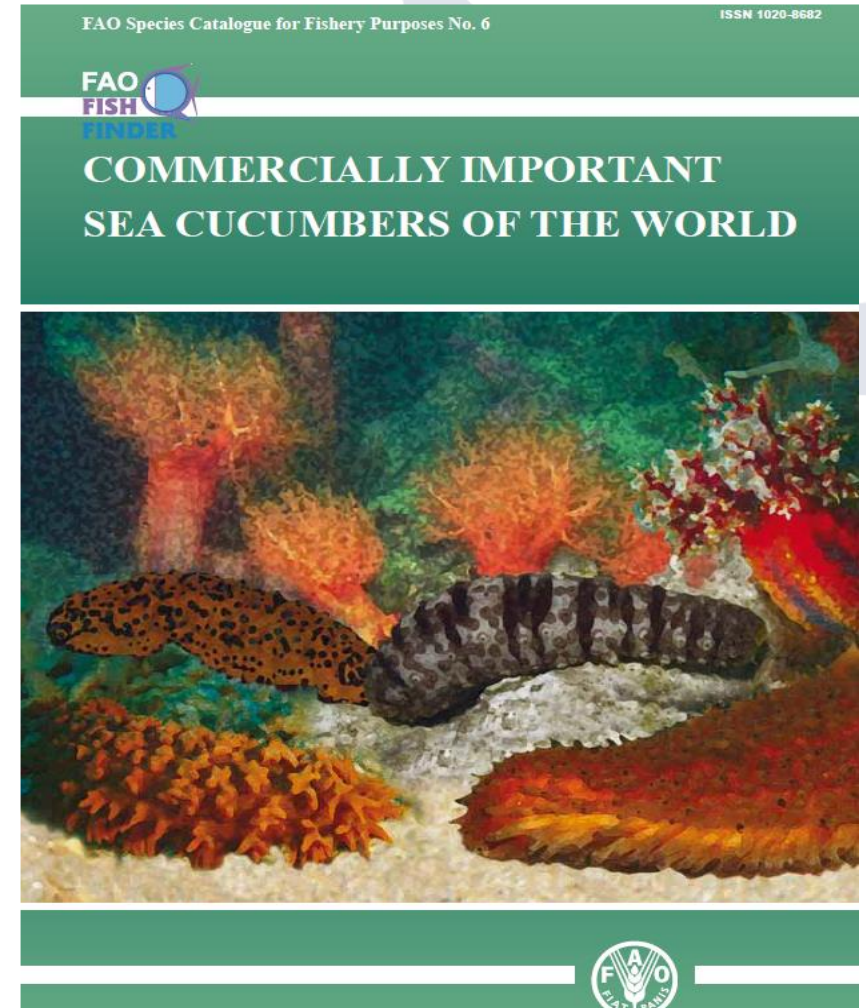
Atlantic & Mediterranean species:

Of commercial interest :

Actinopyga agassizii,
Holothuria Mexicana,
Astichopus multifidus,
Isostichopus badionotus,
Cucumaria frondosa,

Emerging species:

Parastichopus tremulus,
Parastichopus regalis,
Holothuria polii,
Holothuria mammata,
Holothuria tubulosa,
Holothuria forskali,
Holothuria arguinensis.





Recent bibliographic review with meta-analysis, carried out in the period 06/2021 -03/2022

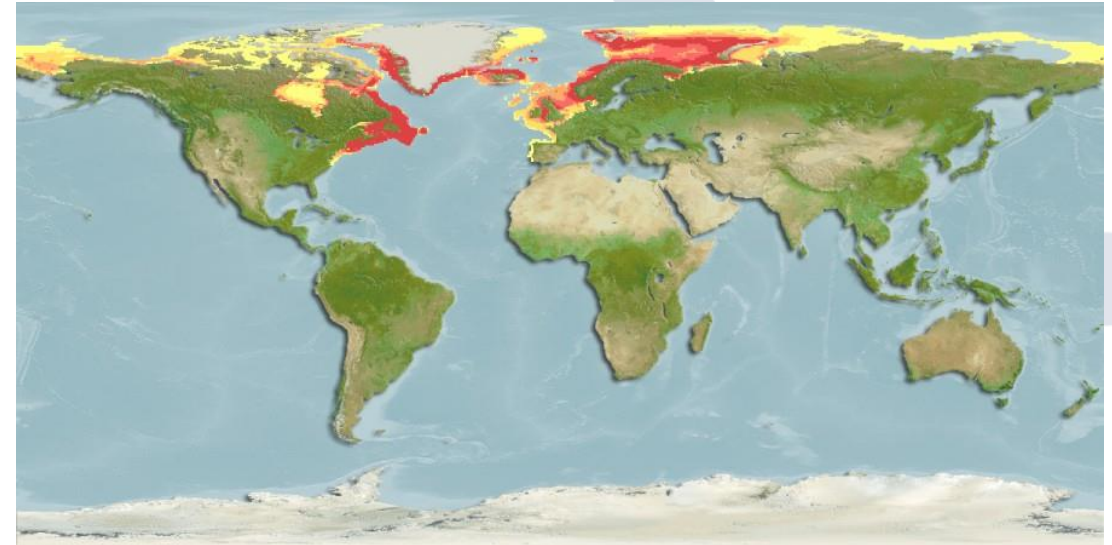
In preparation for early 2023 – A multi-species book with 50+ chapters
The World of Sea Cucumbers – Challenges, Advances and Innovations

Editors: Annie Mercier, Jean-François Hamel, Chris Pearce, Andy Suhrbier

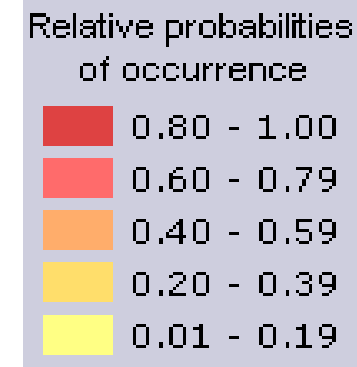
- Sea cucumber genomic information has been partially studied and there are to date 11 full genome assemblies published in the NCBI database, namely of *Chiridota heheva*, *Australostichopus mollis*, *Paelopatides confundens*, *Actinopyga echinites*, *Apostichopus leukothele*, *A. californicus*, *A. parvimensis*, *A. japonicus*, *Holothuria glaberrima*, *H. tubulosa*, *Stichopus horrens*.
- Only 5 belong to temperate or coldwater environments - *Chiridota heheva*, *Paelopatides confundens*, *Apostichopus leukothele*, *Apostichopus californicus* and *Holothuria tubulosa*
- Genomic information for most other sea cucumber species is limited to the mitochondrial genome level, or to availability of information on basic taxonomically relevant genes (Yang et al., 2020).

Most widely distributed sea cucumber species in the North Atlantic & North Pacific & Mediterranean

- According to SeaLifeBase, World Register of Marine Species (WoRMS), IUCN Red List of Endangered Species, the Catalogue of Life (COL), EMODNET (GBIF/OBIS) as sources some of the most widely distributed temperate/ cold water sea cucumbers are ***Cucumaria frondosa***, ***Parastichopus regalis***, ***Parastichopus tremulus***, ***Holothuria grisea***, ***H. arguinensis*** and ***Aslia lefevrii***



- According to the same data sources ***H. tubulosa***, ***H. forskali***, ***H. mammata***, ***H. poli*** and ***Thyone fusus*** are more abundant in the Mediterranean, Black Sea and/ or Red Sea, although often present in the Atlantic.



Most widely distributed sea cucumber species in the North Atlantic & North Pacific & Mediterranean



Holothuria tubulosa



Holothuria forskali



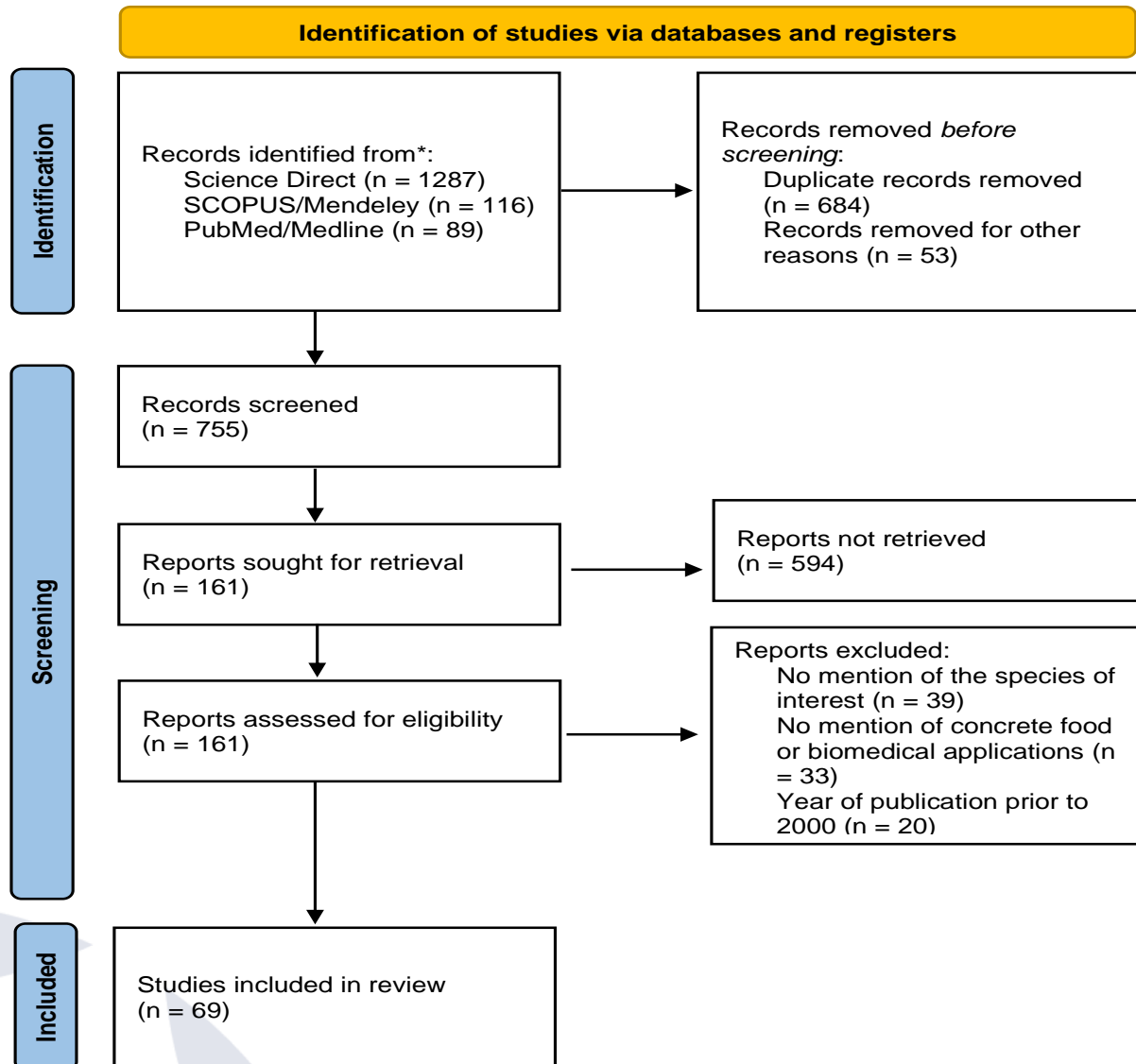
Parastichopus tremulus

Focus of the meta-analysis on the Atlantic species *Cucumaria frondosa*, *Parastichopus tremulus*, *Holothuria tubulosa* and *Holothuria forskali*

MAIN FOCUS OF THE REVIEW ON AVAILABLE KNOWLEDGE ON THE BIOTECHNOLOGICAL AND FOOD APPLICATIONS:

- Biomedical tissue regenerative potential of NA sea cucumber collagen
- Food applications of sea cucumber collagen fractions
- Structures and functions of known bioactives
- Associated microbiota
- Cell cultures from echinoderms/ sea cucumbers

Sea cucumber collagen in tissue regeneration, review in agreement with PRISMA guidelines



Most available information is on the tropical species, and on *Cucumaria frondosa* (Hossain, Dave and Shahidi, 2020 and Senadheera and colleagues, 2020); however, no current commercial or confirmed in vivo tissue regenerative applications exist for *C. frondosa* collagen products

H. tubulosa collagen has been tested in vitro at lab scale for human fibroblast culture under the form of a membrane product for guided tissue regeneration (Ferrario et al., 2016).

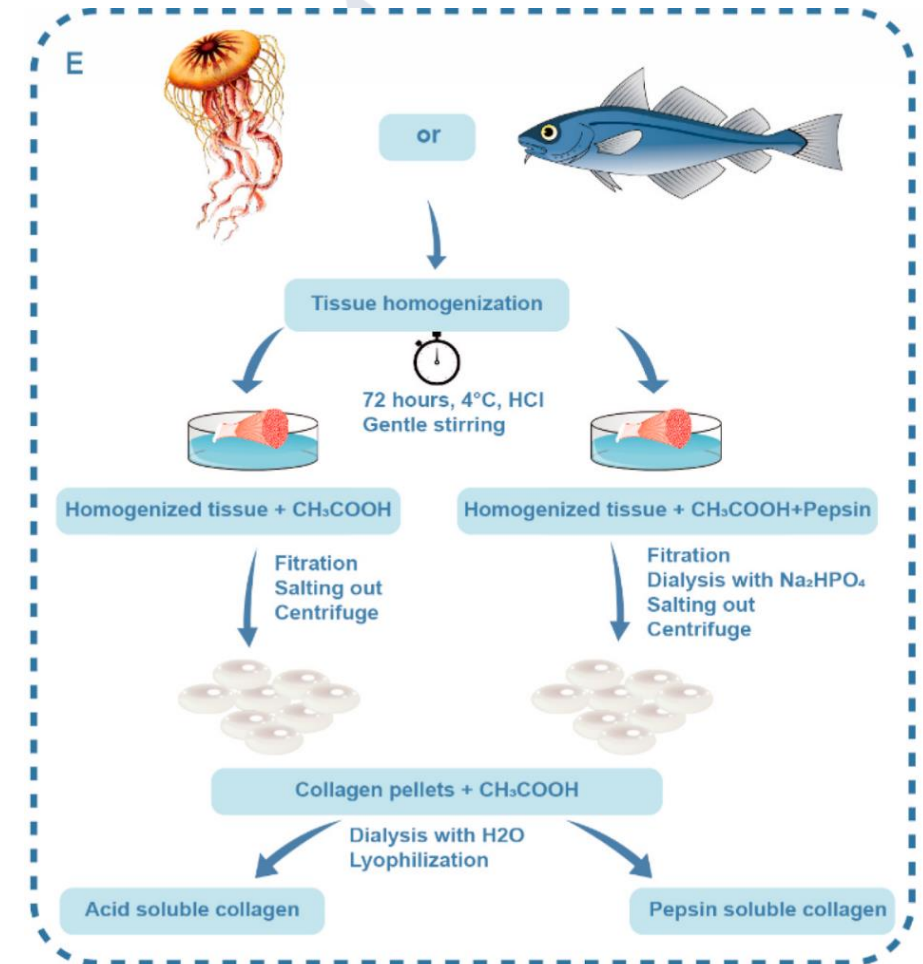
The adhesive collagen-associated biomaterials in the Cuvierian tubules of *H. forskali* have also been structurally characterized as potential biomedical product (Demeuldre et al., 2014).

P. tremulus collagen-derived peptides are under study for functional hydrogel development (Mildenberger et al., 2021).

Sea cucumber collagen – structural specificities and extraction methods

Characteristics	Sea Cucumber Derived Collagen	Mammalian Collagen
Abundant type	Type I collagen	Type I collagen
Differences in amino acid composition	Low hydroxyproline content, high glutamic and aspartic acid residues	High hydroxyproline content, low glutamic acid and aspartic acid residues
Covalent cross links	Internally present and provide stabilization to the molecule	Internally present and provide stabilization to the molecule
Thermal stability	Low thermal stability with low denaturation temperature compared to mammalian collagen	High thermal stability compared with high denaturation temperatures
Resistance to protease digestion	Relatively low	Relatively high
Gel forming ability	Comparatively low	Comparatively high
Moisture absorption ability	Relatively high	Relatively high

Major distinctive characteristics of sea cucumber collagen in comparison to mammalian collagen (from Senadheera et al., 2020)



Review of collagen extraction processes for producing acid-soluble and pepsin-soluble marine collagen (from [Wan et al., 2021])

Sea cucumbers contain a variety of compounds with of biological and pharmacological activities

- Sulphated polysaccharides
 - Chondroitin sulfate
 - Fucoidans
- Triterpene glycosides
 - Frondosides in *C. frondosa*
- Collagen, peptides and amino acids,
- Carotenoids
- Vitamins, minerals
- Cerebrosides, fatty acids
- Phenolic compounds

Table 3. Biologically active compounds of Atlantic sea cucumber and their functions.

Bioactives	Body Parts	Biological and Medicinal Effects	Extraction and Isolation Method	References
Fucosylated chondroitin sulfate	Body wall	Antithrombotic, anticoagulant, anticancer, anti-inflammatory, antitumor, antidiabetic, anti-osteoarthritis, alleviates inflammation, alleviates pain, and improve immune system	Enzymatic (papain/ Alcalase) hydrolysis followed by precipitation (cetylpyridinium chloride/ ethanol/ sodium hydroxide/ trichloroacetic acid)	[57,93,99]
Collagen	Body wall	Antihypertension, antiaging, anti-wrinkle, alleviates skin problems, and wound healing	A divalent cation chelator (EDTA) followed by extraction in water	[79,80]
glycosides (saponins)	Body wall	Antibacterial, antifungal, antiviral, antitumor, anticancer, antiangiogenic, and photo-protective	Isopropyl alcohol/ water extraction and refluxing with chloroform/ methanol/ethanol	[83,100,101]
Fucoidan	Body wall	Anticoagulant, antibacterial, antiaging, anti-hyperglycemic, lowering blood glucose level, and photo-protective	Hydrolysis with papain and precipitation with cetylpyridinium chloride	[58,70]
Phenolic compounds	Body wall, tentacles, and viscera	Antioxidants and antibacterial	Solvent extraction (methanol), water, organic solvent (ethyl acetate) and a mixture of water/ miscible organic solvent (acetonitrile)	[16,54]
Cerebrosides	Body wall	Anticancer, anti-inflammatory, and anti-adipogenic activity	Solvent extraction (65% ethanol) and isolated by High-performance liquid chromatography (HPLC), extracted by chloroform/ methanol using high speed counter-current chromatography	[19,102,103]
Amino acid	Body wall, tentacles, and viscera	Anti-fatigue, repairing tissue, nutritional storage, and wound healing	Reversed phase HPLC	[54,55]
Protein (bioactive peptide)	Body wall	Antimicrobial	Fractionated utilizing ammonium sulfate precipitation and analyzed by size exclusion chromatography	[32]
Vitamin and minerals	Body wall, tentacles, and viscera	Cosmeceutical properties, promote healthy growth and metabolism, lower the blood sugar level	Association of Official Analytical Chemists (AOAC)-and inductively coupled plasma mass spectrometry (ICP-MS)	[55,93]
Omega-3 (EPA)	Body wall, tentacles, and viscera	Anti-hyperglycemic, decrease cholesterol, and protect the heart	Solvent extraction (methanol: chloroform: water) and analyzed by gas chromatography (GC)/ HPLC	[50,54,55,104]

Source for bioactive compounds

- The health benefits of the sea cucumbers have been known for centuries.
- Interest in their ingredients has increased in recent years
- A number of scientific papers has been published
- Further research and development
- Request for seacucumbers will only grow.
- Market for different products will grow and new markets will be established

Known activities

- Anticancer
- Anti-angiogenic
- Anti-inflammatory
- Antidiabetic
- Anti-coagulation
- Antimicrobial
- Antiviral
- Antioxidation
- Anti-osteoclastogenic properties

Icelandic sea cucumber products from different providers



Capsules with *Cucumaria frondosa* extracts are popular supplements in Iceland



Arctic Star sea cucumber capsules contain more than 50 types of nutrients, high in collagen, 18 types of amino acids, taurine, chondroitin sulphate, polypeptides, calcium, phosphorus, iron, iodine, zinc, selenium, vanadium, manganese, vitamins B1, B2, B3, B5 and more

***Cucumaria frondosa* extract** rich in collagen, zinc, iodine and iron. Contains bioactive chondroitin sulphate and saponin

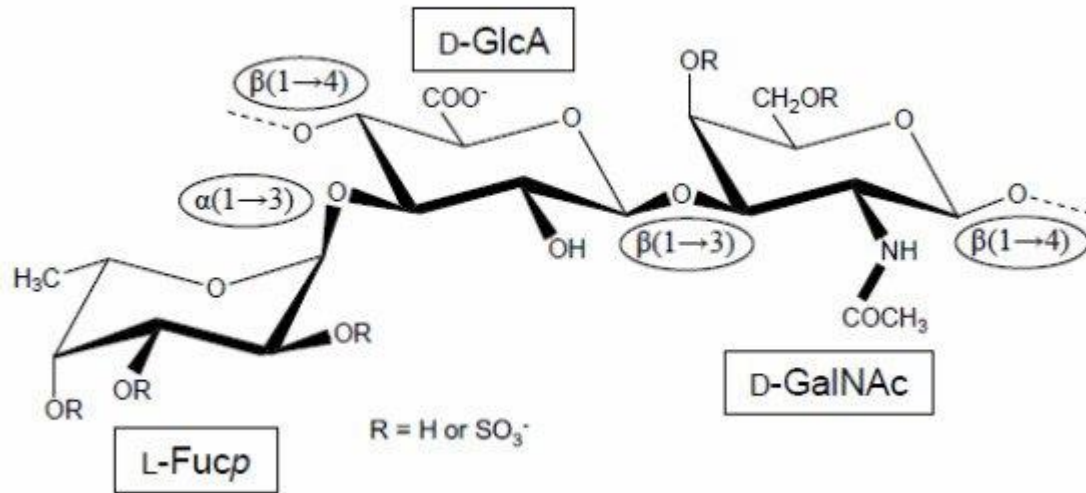
Unique source of health promoting compounds

- The sea cucumbers contain compounds with specific structures only found within sea cucumbers / *Holothuroidea*
- These specific structures contribute to the bioactive properties, making sea cucumbers a unique source of health promoting ingredients



Figure from <https://innocentseas.com/>

Sea cucumber polysaccharides



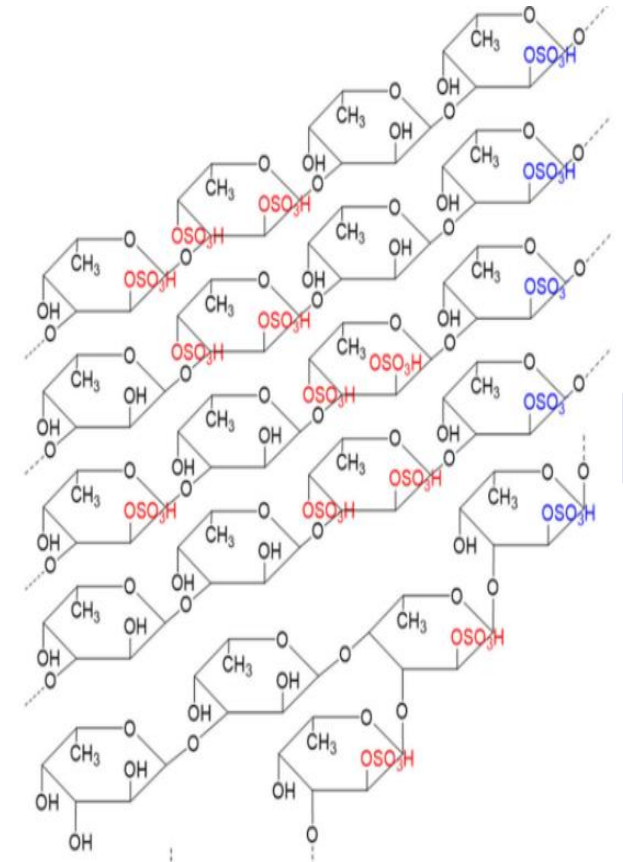
Leptopentacta grisea,
Holothuria tubulosa

Acaudina molpadioides

Isostichopus badionotus

Thelenota ananas

Apostichopus japonicas



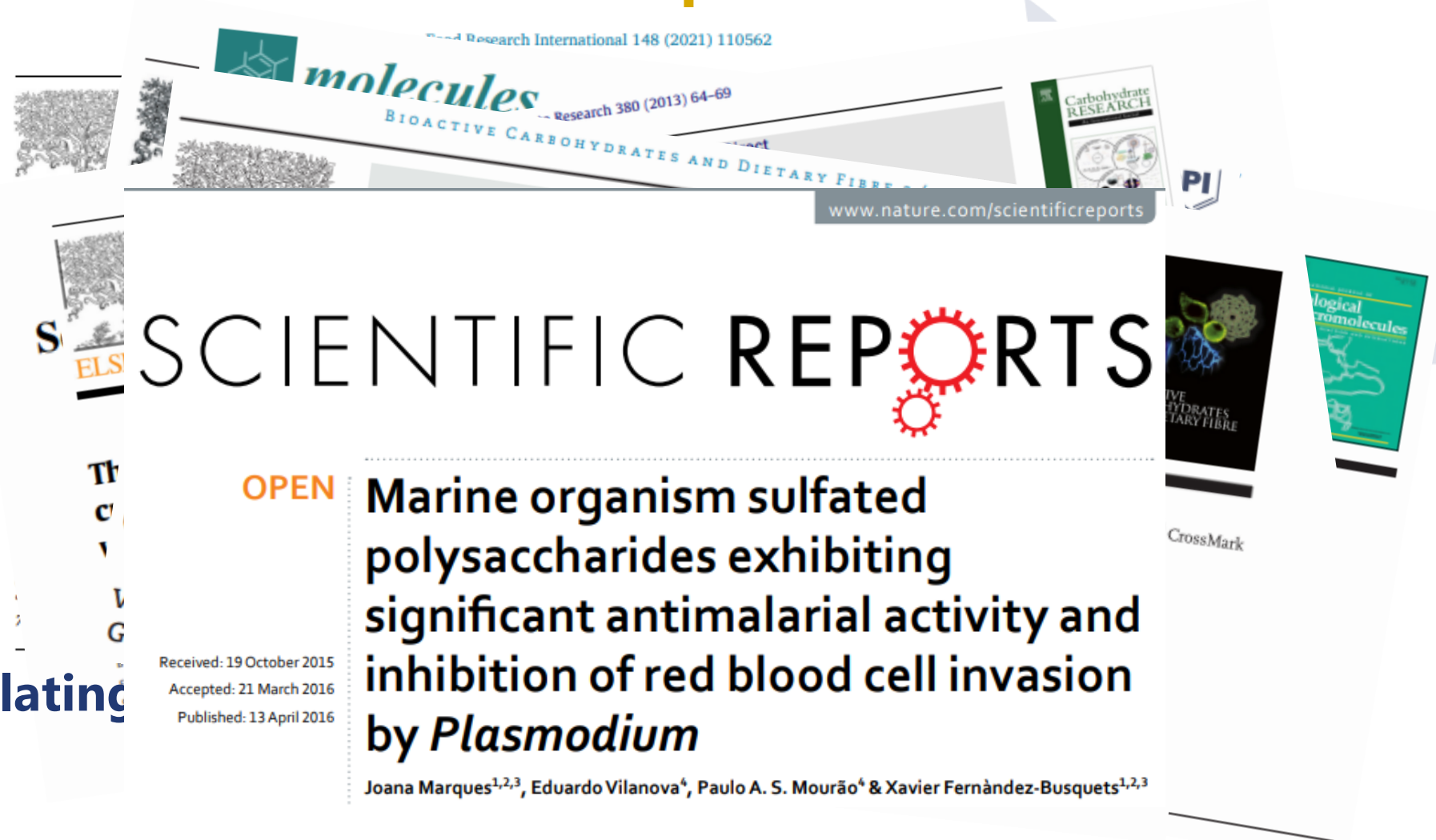
- Fucosylated chondroitin sulfate

- Sulfated fucoidan

Sulfation pattern and extent is of great importance regarding bioactivity

Polysaccharides - neutraceutical and pharmaceutical activities

- Prebiotic
- Anti-diabetic
- Anti-cancer
 - Tumor growth
 - Metastasis
 - Angiogenesis
 - Boosting effect
- Anti-viral
- Immunomodulating
- Anti-malaria

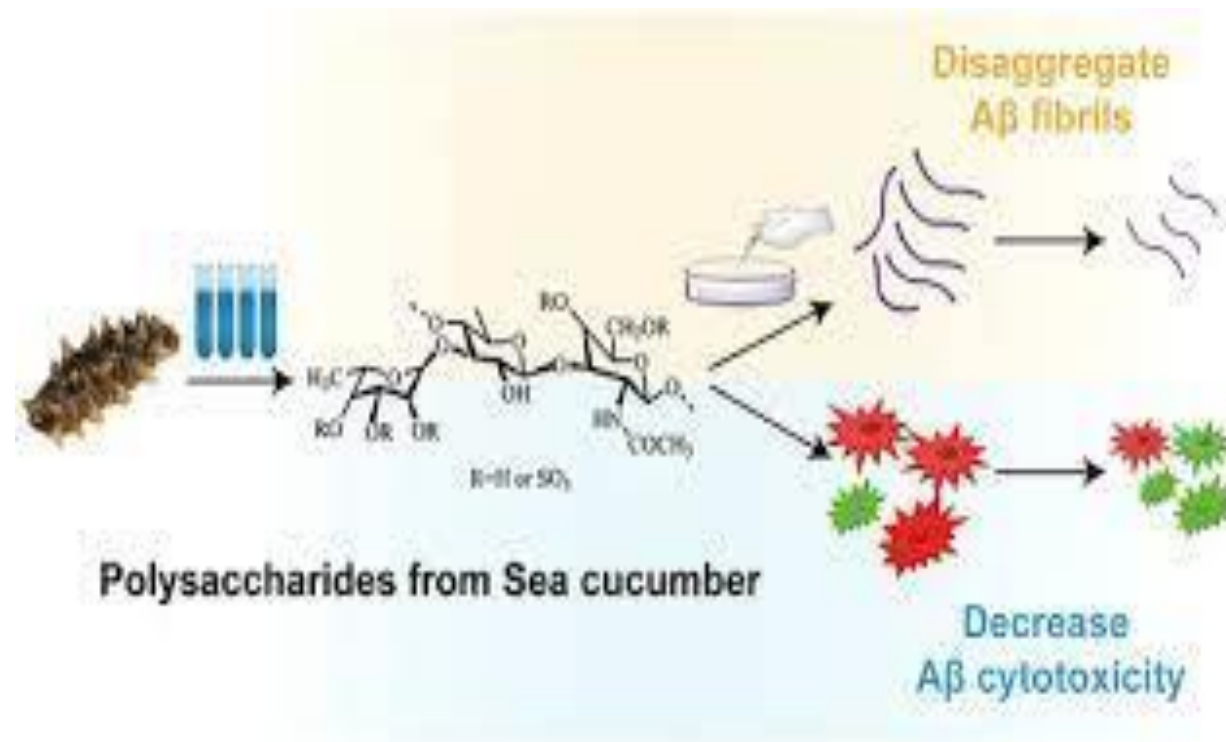


Inhibitory Effects of Sulfated Polysaccharides from the Sea Cucumber *Cucumaria Frondosa* against A β 40 Aggregation and Cytotoxicity

ACS Chemical Neuroscience (IF4.418), Pub Date : 2021-05-17, DOI: [10.1021/acscemneuro.1c00223](https://doi.org/10.1021/acscemneuro.1c00223)

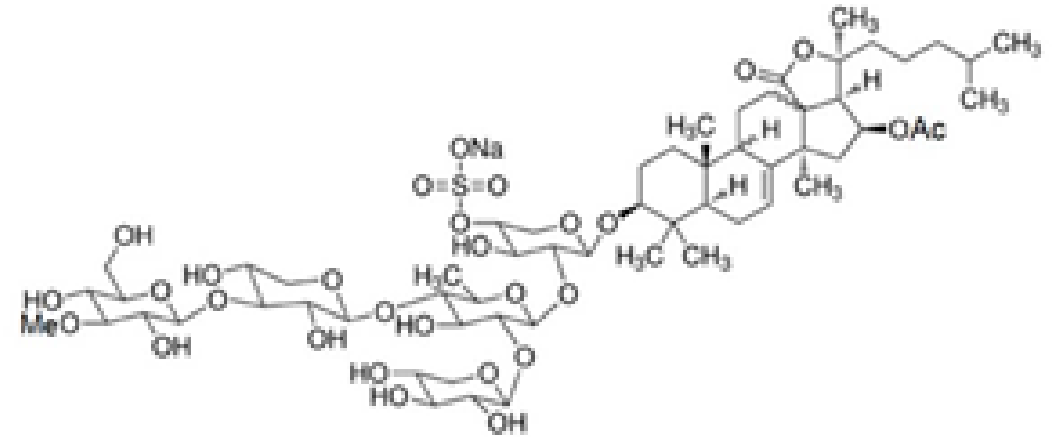
Gao Li, Yu Zhou, Wu-Yue Yang, Chen Zhang, Liu Hong, Lee Jia

Anti-Alzheimer activities



Triterpenoid saponins - Frondoside A

- One of the most studied compounds from *C. frondosa*
- Broad anti-cancer activity
- Triterpenoid glycosides-saponins
- Abundant secondary metabolites
- Chemical defense mechanism
- Low cytotoxicity, still effective against different cancer cells



Anti-cancer activity

- Pancreatic cancer
- Human breast cancer
- Lung cancer
- Leukemia
- Burkitt lymphoma
- Prostate cancer

Other activities:

- *Immunomodulatory activity*
- *Neurodegenerative disorders such as Alzheimer and Parkinson*



Bioactive compounds from sea cucumber associated microbiota



MØREFORSKING



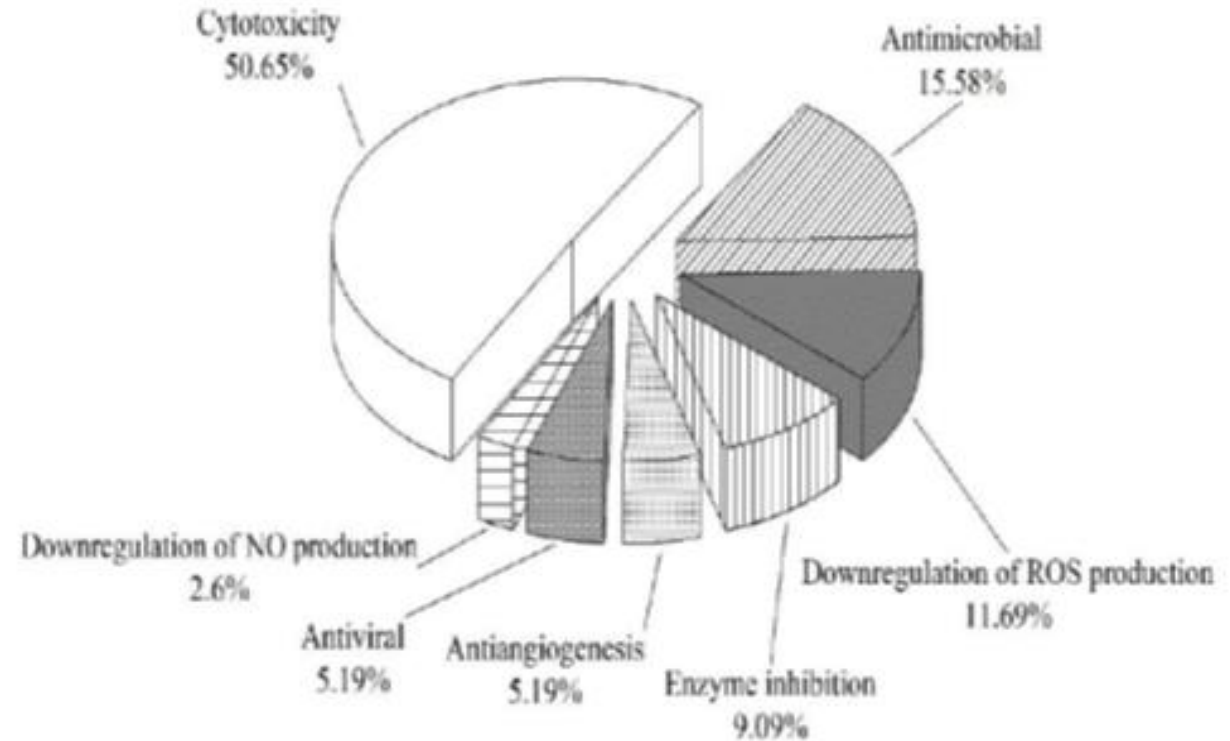
NORA



A systematic search in SCOPUS/MENDELEY with keywords “sea cucumbers” and “microbiota” yielded 65 articles, published in the period 2014-2022. From these 45 were focusing on the associated microbial communities of sea cucumbers and 40 of these were focused the tropical species *Apostichopus japonicus* (89% of all publications).

2 articles in SCOPUS on *Holothuria glaberrima* microbiota (Diaz-Diaz et al., 2021; Pagan-Jimenez et al., 2019)

1 article studying the composition and biotechnological potential of the intestinal microbiota of *H. forskali* and *H. tubulosa* (Leon-Palmero et al., 2018)



Review of the natural products derived from tropical sea cucumber associated microbiota: percentage distribution of the isolated natural products. [Chen et al., 2021]

Main message

- Ingredient for the development of new drugs and functional foods
- High market potential
- Sustainable fisheries compromised
- Stock management measures needed
- Need for developing aquaculture systems

