

From buds that may not burst - Marine Biotechnology in Europe

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Content

- 1. Innovation potential of living marine resources**
- 2. Turning knowledge into products - own experiences**
- 3. Ocean's integrity and biodiversity is the basis for a wealthy society**

Innovation potential

- predominantly **unexplored** oceanic regimes
→ expectation of a vast amount of new natural substances
- highly developed **(bio-)chemical mechanisms** for defense and reproduction ($2,7 * 10^9$ years more „experience“)
- **Congruences** of mineral and trace element composition in human cell fluid and ocean
- **Biodiversity**: all 33 animal clades live in the sea, 15 on land

What is the Monetary Value of Ocean's Biodiversity ?

Ecosystem service value:

*US \$ 563 billion – 5.69 trillion
for anti-cancer drugs of marine origin*

(Erwin et al. 2010)

Algae-based active ingredients

- minerals, salts
- trace elements
- special polysaccharides
- polyphenols
- special amino acids
- vitamins
- carotinoids
- **other** secondary phytochemicals and antioxidants

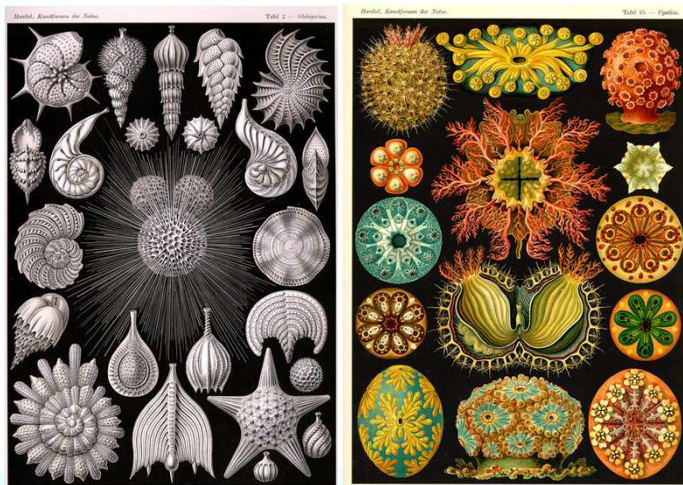


Turning knowledge into products: oceans are a treasure trove for innovations

Structures / functions
in nature

Academia
SME/Industry

Consumer's / society's
demands



Erich Haeckel: *Kunstformen der Natur*, 1899-1904

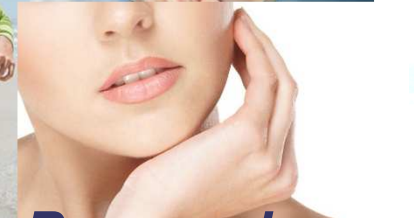
For example:



*Biological
pest control*



Food



Personal care

Demands and trends

Consumer study by Mintel:

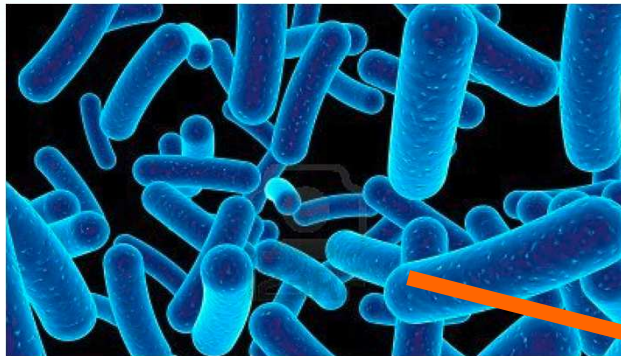


OECD 2017:

healthy living is one of the most important global megatrends

High hostile pressure on algae surface

Grazing, colonising, degrading etc.
→ mechanisms of protection

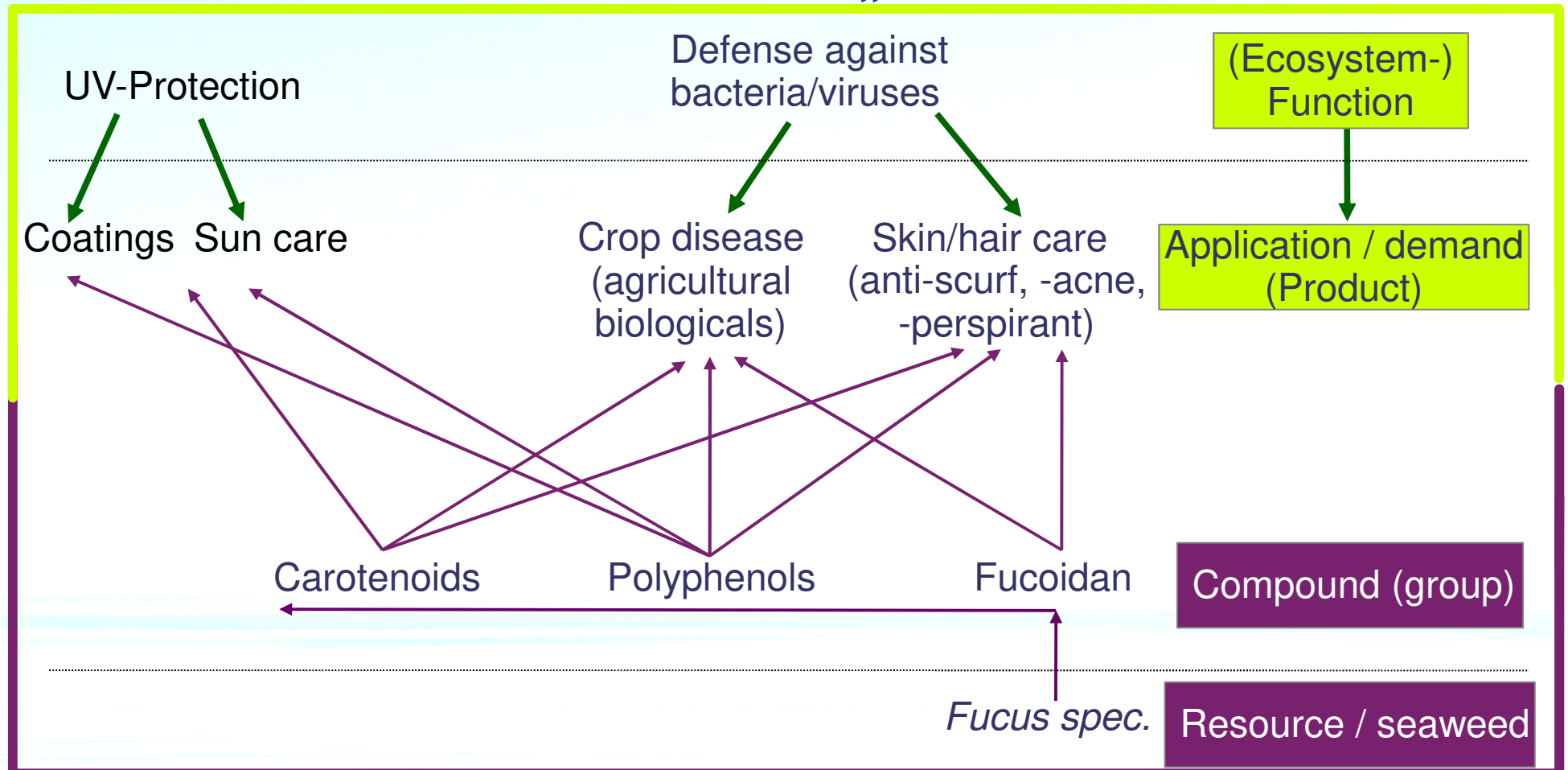


Number of bacteria in sea water:
 $10^6 - 10^9 / \text{ml}$



Systematic approach

Functional scheme „Protection“



Better off blue – let's go!



Products and developments from CRM / oceanBASIS – Examples:

Prevention and protection (#1)

→ Antibacterial activity

Inhibition [%]

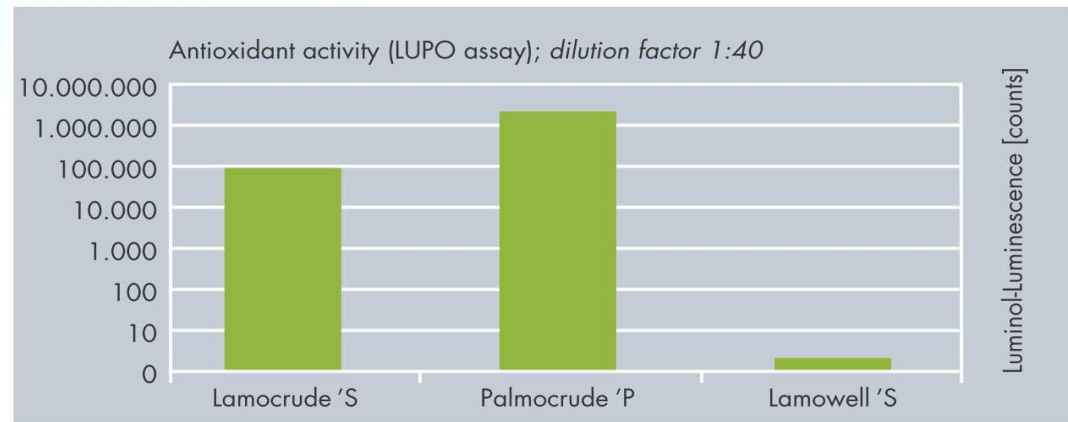
		<i>St. aureus</i>		<i>MRSA</i>		<i>St. epidermidis</i>		<i>Ps. aeruginosa</i>		<i>B. epidermidis</i>	
Commercial Extracts		5%	10%	5%	10%	5%	10%	5%	10%	5%	10%
Lamocrude'S	Ex242	47***	52***	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.
Lamowell'S	Ex243	33	72***	neg.	neg.	neg.	neg.	neg.	34	neg.	neg.
Palmocrude	Ex244	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.
Fucoidan	Ex245	49	41	neg.	26	72	82	30	31	neg.	26
Kollagen	Ex246	34	neg.	neg.	neg.	neg.	neg.	33	29	20	29
Extracts under Development		1%		1%		1%		1%		1%	
CCL16	Ex247	n.b.		96		87		n.b.		n.b.	
AAC148	Ex248	100		100		100		26		neg.	
Control	DMSO	neg.		neg.		neg.		28		20	
AAC 150F	Ex249	n.b.		n.b.		n.b.		n.b.		n.b.	
CLA1	Ex250	n.b.		n.b.		n.b.		n.b.		n.b.	

Algae compounds can strongly inhibit growth of *S. aureus*,
S. epidermis and *MRSA*

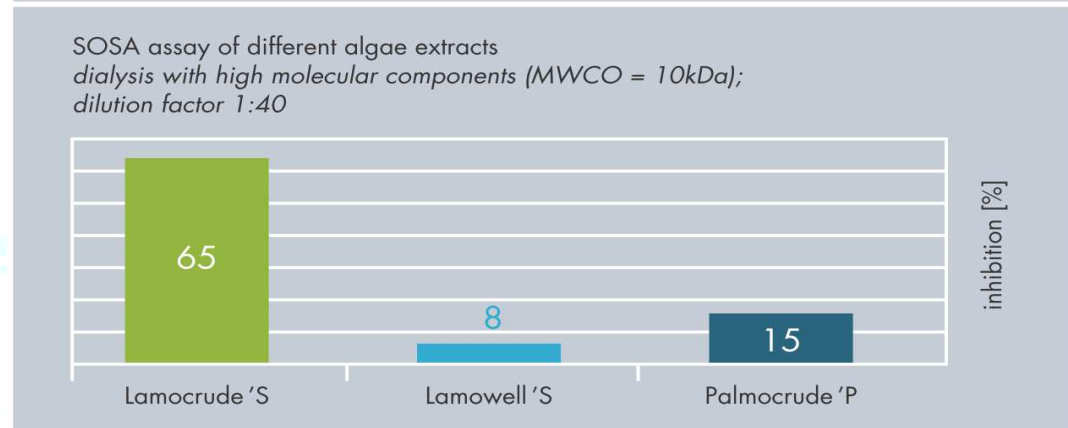
Prevention and protection #2

→ Antioxidant activities

Antioxidant capacity (LUPO)

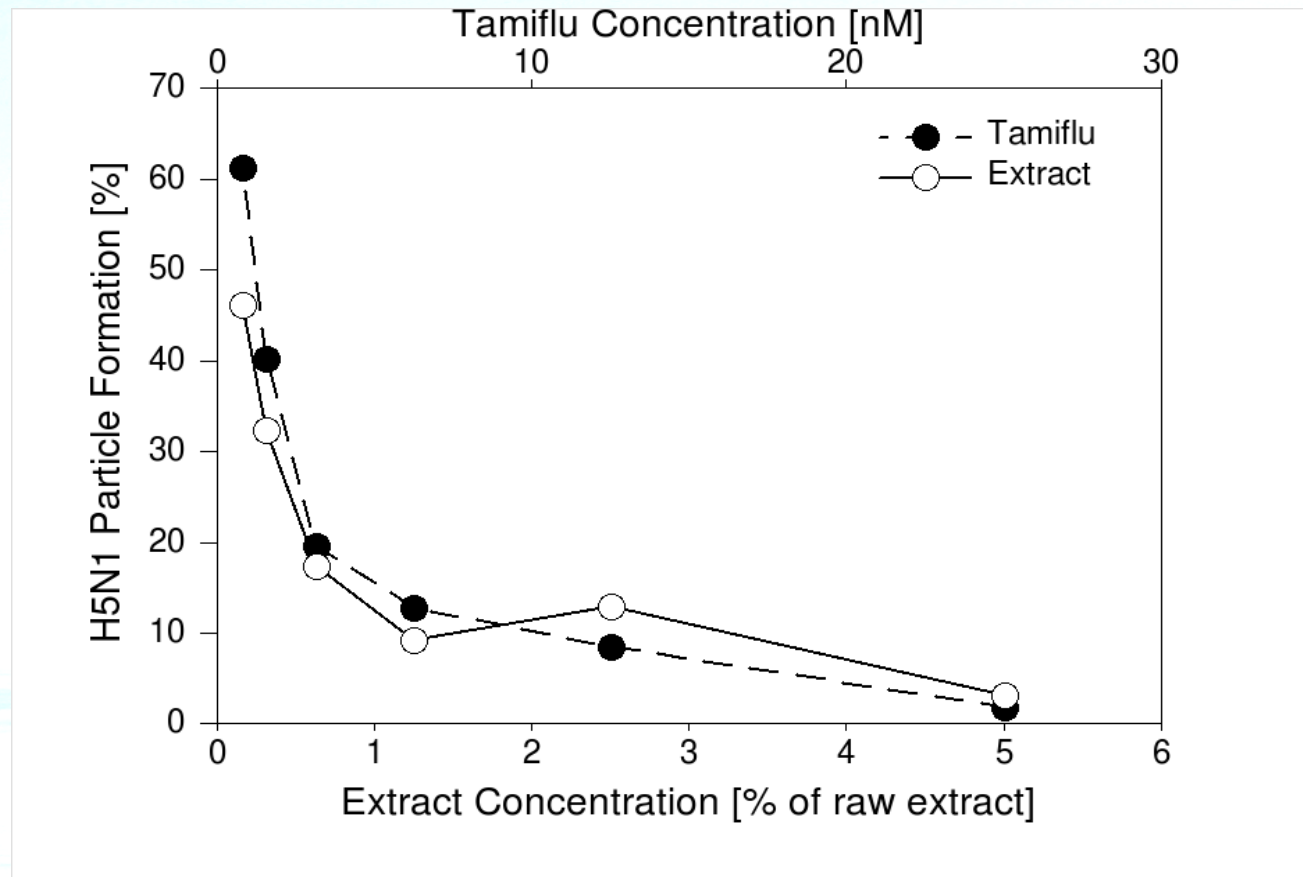


Radical scavenger activity (SOSA)

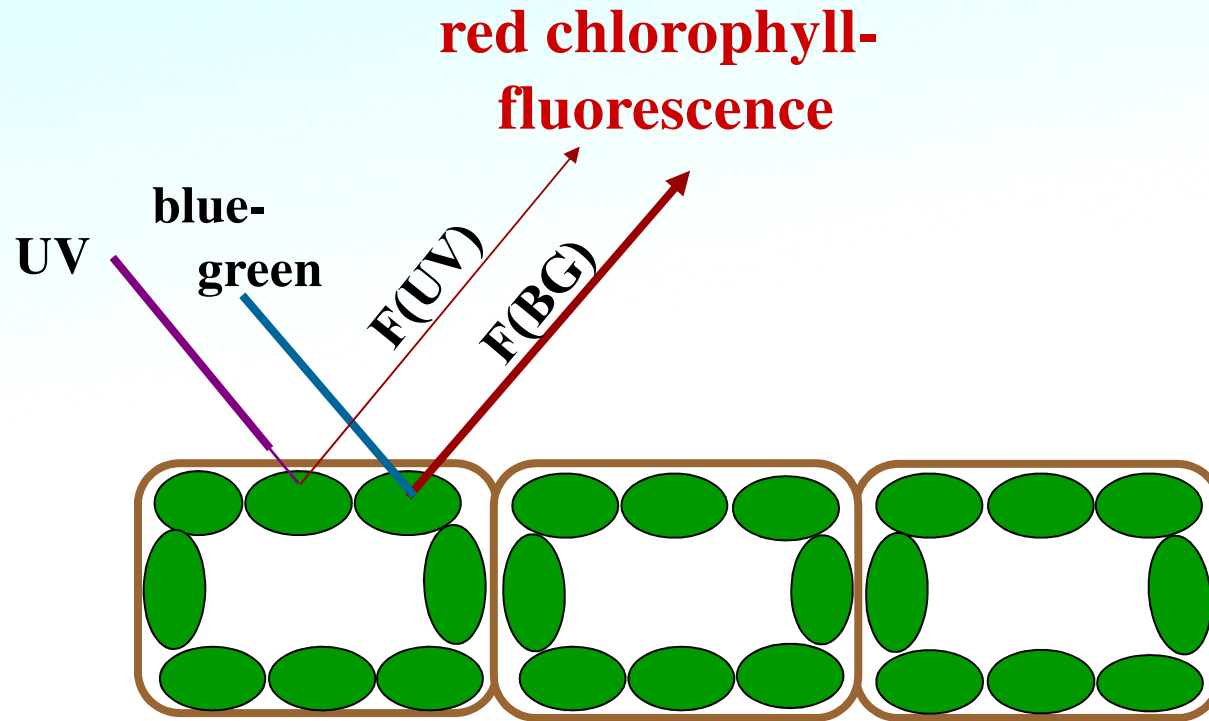


Prevention and protection #3

→ Antiviral activities



#4: Protection against UV-B-radiation



Algae filament with cell wall and chlorophyll

$$F(UV)/F(BG) \rightarrow \text{UV-transmittance}$$

Wir fördern Wirtschaft

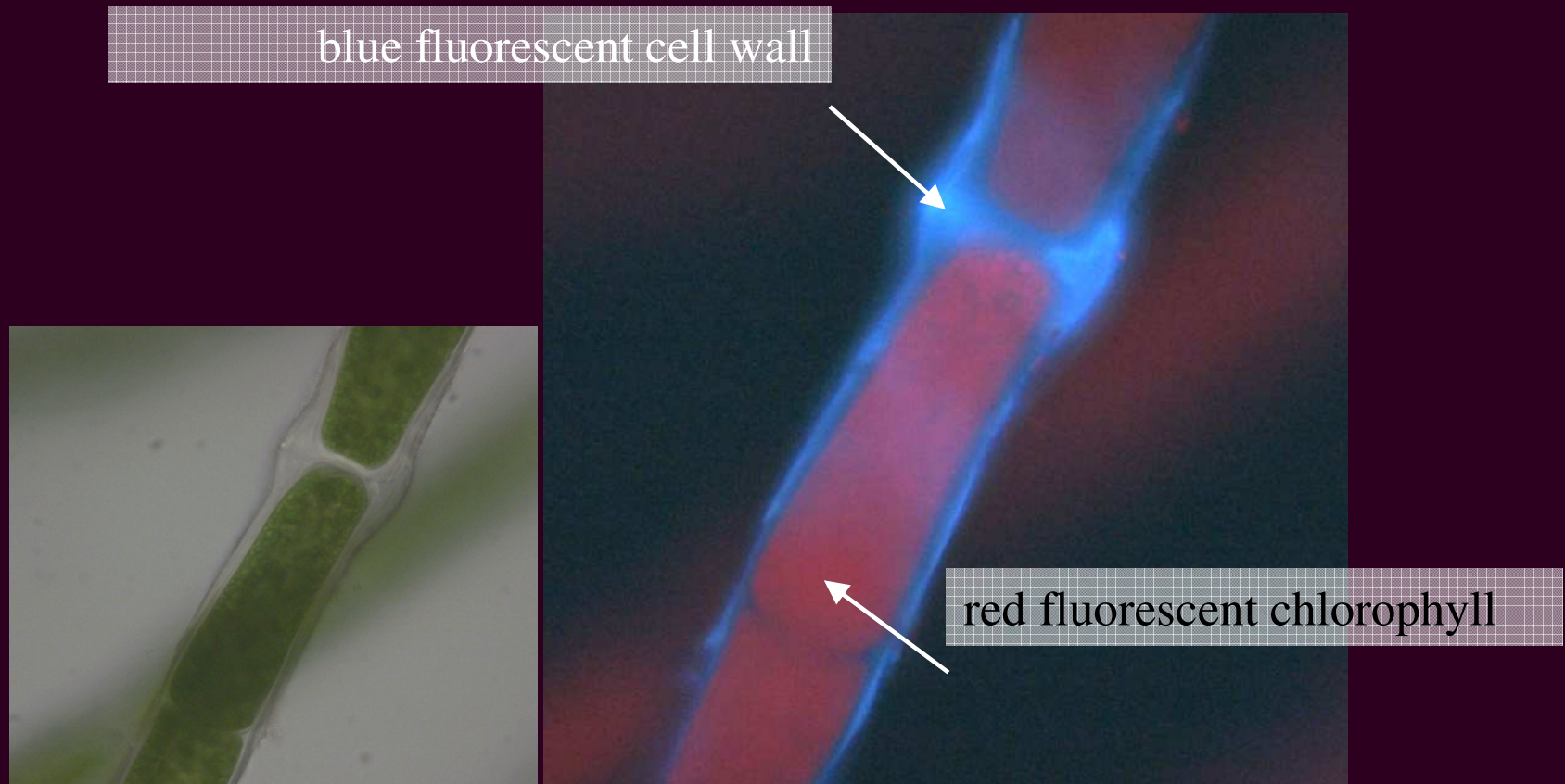


Landesprogramm Wirtschaft: Gefördert durch die Europäische Union - Europäischer Fonds für regionale Entwicklung (EFRE), den Bund und das Land Schleswig-Holstein

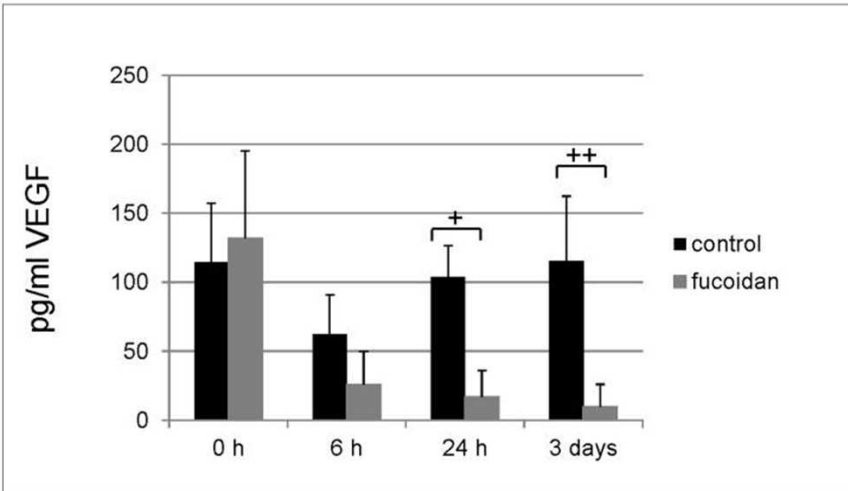
Piker, CRM/oceanBASIS

Better off Blue: Marine biobased materials and chemicals, 28.9.17 Berlin

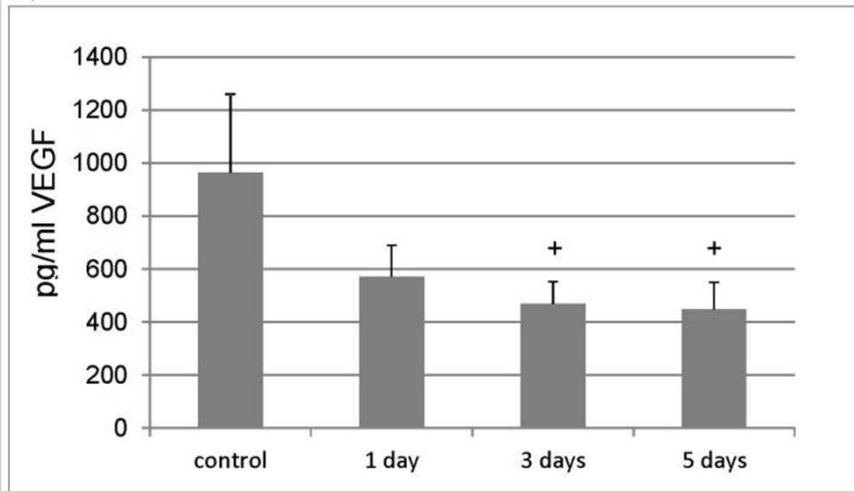
Blue fluorescent UV-protecting agents in *Cladophora* sp.



A) RPE/choroid organ culture



B) ARPE-19

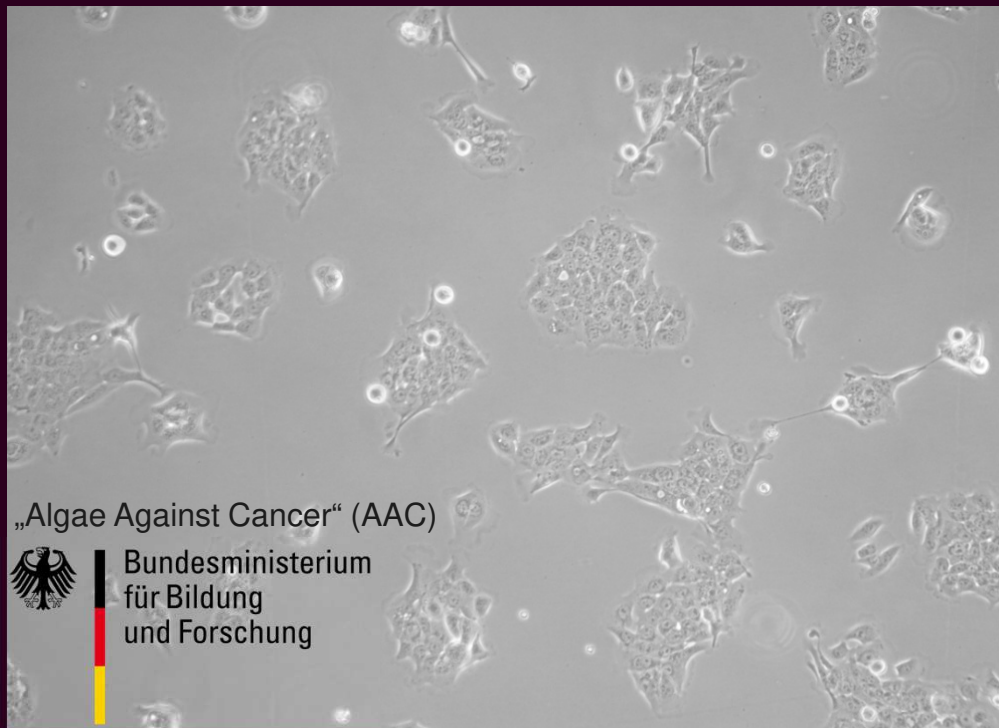


#5: Prevention of aging symptoms (e.g. AMD)

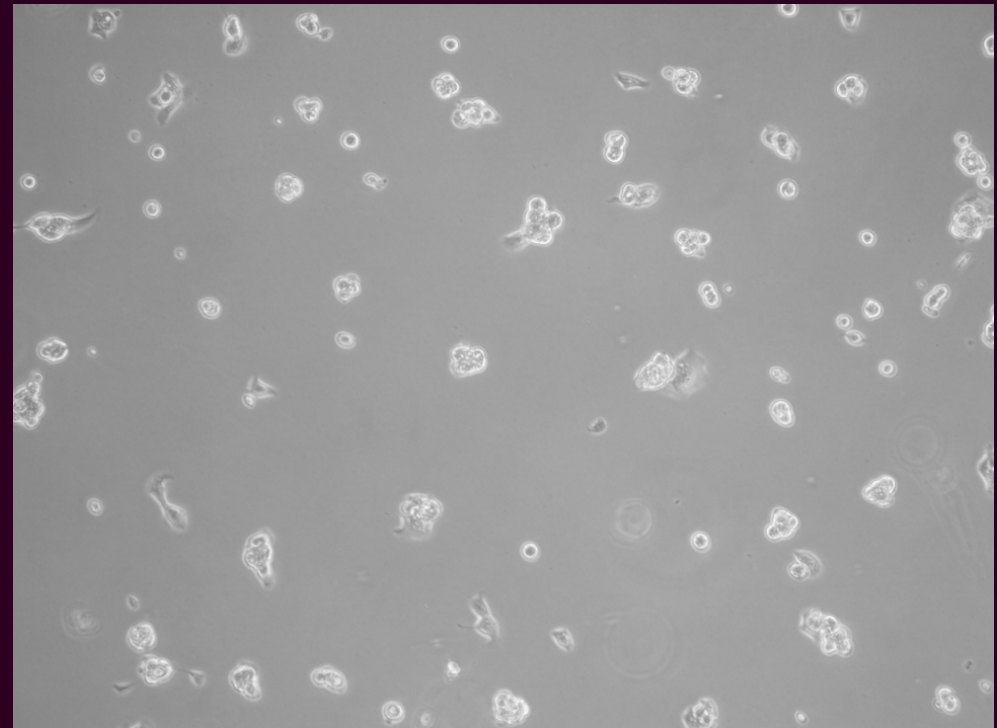
Fucoidan reduces expression of Vascular Endothelial Growth Factor (VEGF) in the retinal pigment epithelium and reduces angiogenesis *in vitro*. (Dithmer *et al.* 2014)

#6: Extract from *Fucus vesiculosus* inhibits growth of pancreatic cancer cells

Control



KF1 extract



(after 24 h incubation)

Geisen *et al.* 2015
Zenthoefer *et al.* 2017

Main marketed products

→ Active ingredients for cosmetic market

Lamocrude 'S

The Natural Brown Algae Extract

Protecting aqueous extract from *S. latissima*, contains unique anti-oxidative algae sugars and polyphenol

Lamowell 'S

The Enhanced Brown Algae Extract

Soothing and nourishing properties. Enhanced bioavailability by long cold fermentation of *S. latissima*.

Qollagen 1%

Collagen from the Deep Ocean

Superior moisturizing properties. Sustainable resource of pure, native collagen.

Palmocrude 'P

The Natural Red Algae Extract

Aqueous extract of *P. palmata*. Improving skin elasticity by promoting cell matrix proteins. Cytoprotective through amino acids and polyphenols.

ocean cosmetics

O
oceanwell

**Marine natural
cosmetics**

- moisturizing,
- protecting
- revitalizing

vegan

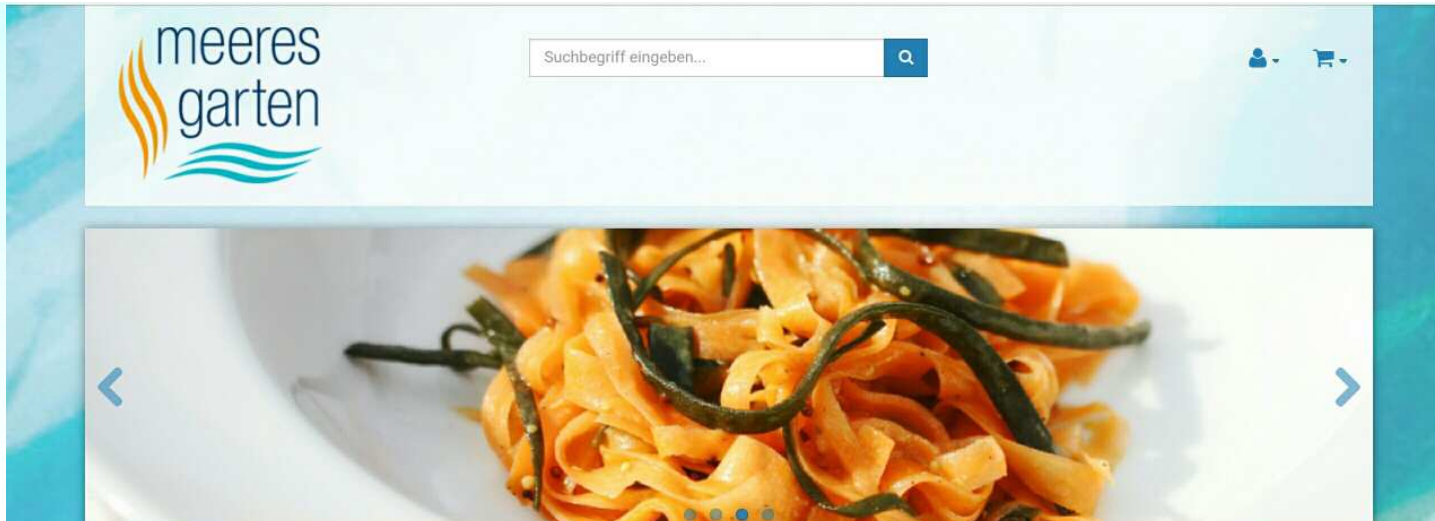


OceanCollagen

ProAge Line

The pure Power of the Sea

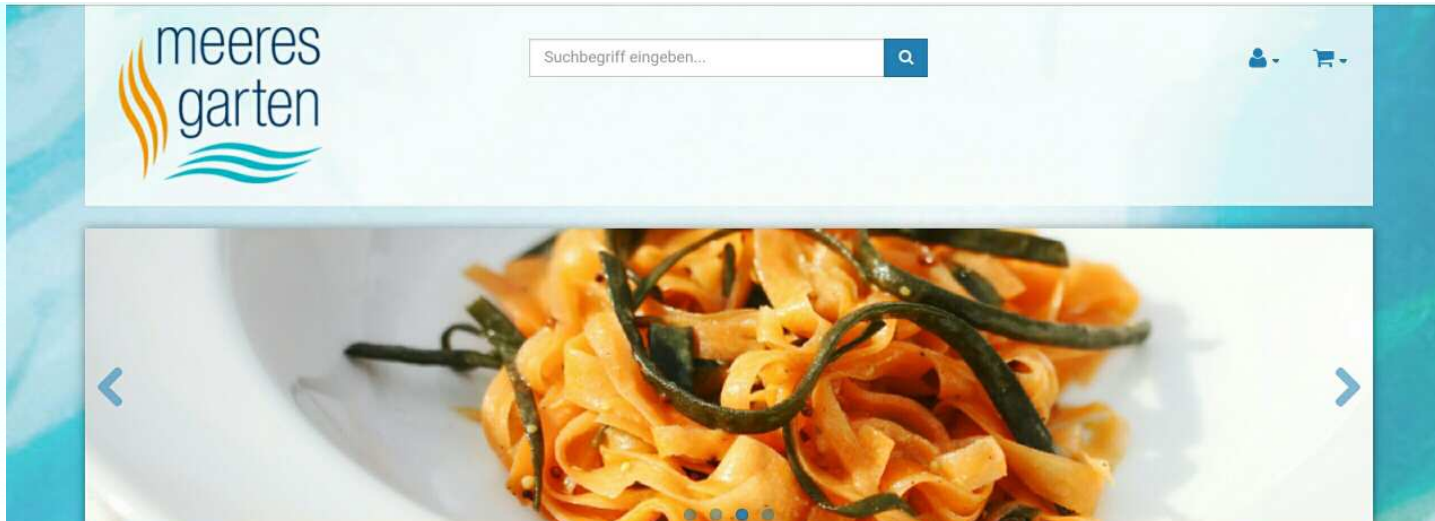




ocean food



Healthy diet and refining cuisine
→ **Seaweed flakes**



ocean food

→ **Natural algae relish**
(„umami“)



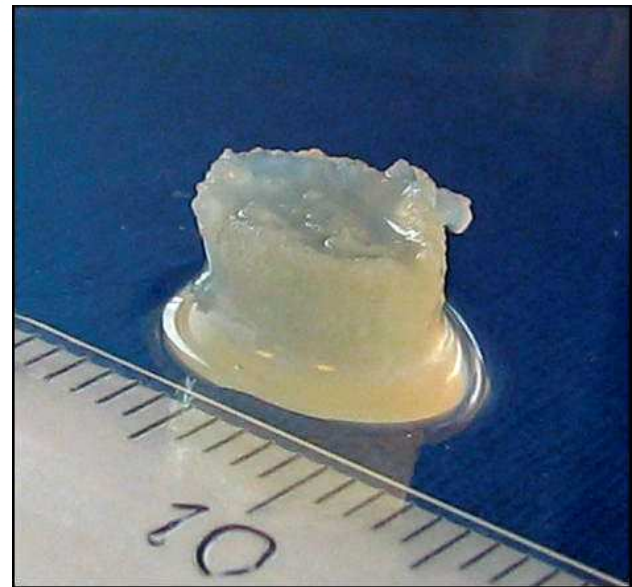
Collagen from marine invertebrates

ocean biotech

Wound healing



Cartilage regeneration



Bioinformatics / „Algaeomics“:

oceanBASIS's first level Algae-Enzyme catalog

EC-number	Algae species/Contig	orient.	homolog. protein	score	perc.ident.	description
EC=1.10.2.2	Eremosphaera_3607	rev	F6H425_VITVI	414	77.78	RecName: Full=Ubiquinol-cytochrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.2.2	FucusVesiculosus_1382	rev	I0Z7G8_9CHLO	750	53.82	RecName: Full=Ubiquinol-cytochrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.2.2	Polysiphonia_12913	for	A8JJ26_CHLRE	662	59.61	RecName: Full=Ubiquinol-cytochrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.2.2	Saccharina_5966	rev	A8JJ26_CHLRE	617	56.00	RecName: Full=Ubiquinol-cytochrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.2.2	SaccharinaNorrisii					chrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.2.2	Ulva_4904					chrome c reductase iron-sulfur subunit; EC=1.10.2.2
EC=1.10.3.3	Polysiphonia_2					dase; EC=1.10.3.3; Flags: Fragment;
EC=1.10.3.9	FucusVesiculosus					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.3.9	Polysiphonia_2					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.3.9	Porphyridium_9					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.3.9	Saccharina_579					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.3.9	Spirulina_1318					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.3.9	Ulva_897					(B) protein; EC=1.10.3.9; AltName: Full=32 kDa thylakoid
EC=1.10.9.1	Ulva_11514					f complex iron-sulfur subunit, chloroplastic; EC=1.10.9.1
EC=1.10.99.1	Eremosphaera					f complex iron-sulfur subunit; EC=1.10.99.1;
EC=1.10.99.1	FucusVesiculosus					f complex iron-sulfur subunit; EC=1.10.99.1;
EC=1.10.99.1	Polysiphonia_1					f complex iron-sulfur subunit; EC=1.10.99.1;
EC=1.10.99.1	Ulva_6218					f complex iron-sulfur subunit; EC=1.10.99.1;
EC=1.1.1.100	Eremosphaera					hydrogenase, putative; EC=1.1.1.100;
EC=1.1.1.100	FucusVesiculosus					-carrier-protein] reductase, putative; EC=1.1.1.100;
EC=1.1.1.100	Polysiphonia_23806	rev	B9TN94_RICCO	225	41.60	SubName: Full=3-oxoacyl-[acyl-carrier-protein] reductase, putative; EC=1.1.1.100;
EC=1.1.1.100	Saccharina_23600	rev	B9TAF7_RICCO	448	40.40	SubName: Full=3-oxoacyl-[acyl-carrier-protein] reductase, putative; EC=1.1.1.100;

Proteins

1639

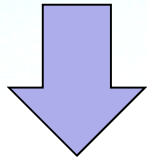
Based on green plant
homologous proteins only

EC-numbers

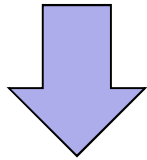
610

A straightforward way to go from candidate sequences to protein:

Candidate transcript
sequence: ORF



Gene synthesis

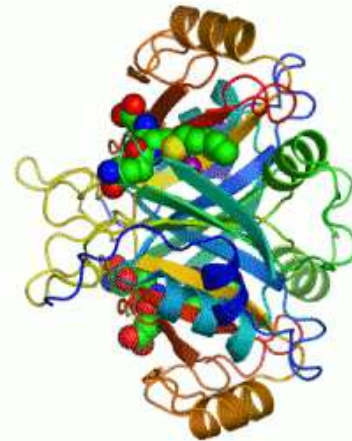


CFS: Cell-Free protein expression

Pharma

Food

Cosmetics



**< 1 mg
protein**

Challenges and bottlenecks

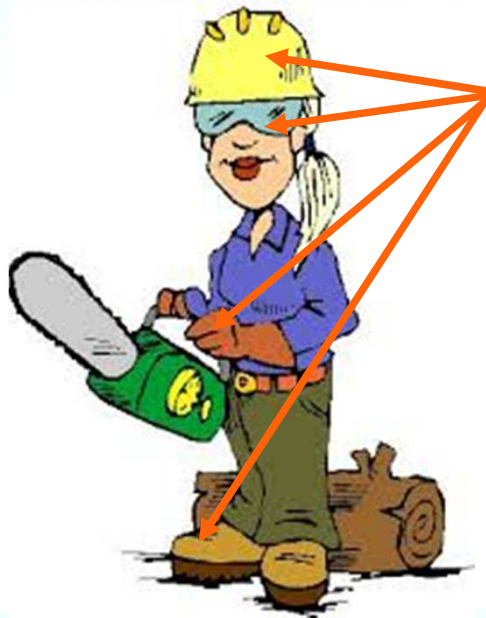


Technology

Technology: Seaweed Processing, Extraction



Challenges and bottlenecks



Safety!

Safety: Medical products



ISO 10993:
**Standards for evaluating the
biocompatibility of medical devices**

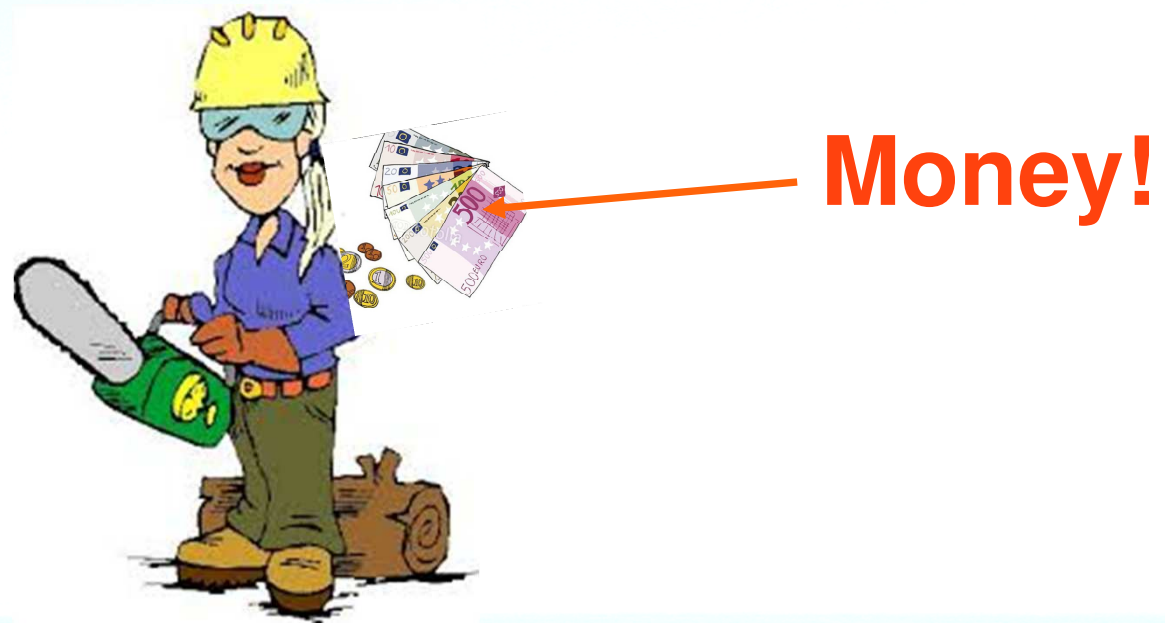
Safety: Personal care products

Self-Documentation showing that the product contains nothing harmful:

- **Safety data sheet**
- **Product specification**
- **GRAS – Generally Recognised As Safe**

(- Toxicity)

Challenges and bottlenecks



Money: No risk no success

- Innovation slump: Dramatic decrease of innovative SME in Germany, 2015:

-20%

- Mainly due to

lack of risk capital

(Actual **Innovation Report** of KfW)

Challenges and bottlenecks



**Nature and
natural
resources!**

Project „FucoSan“

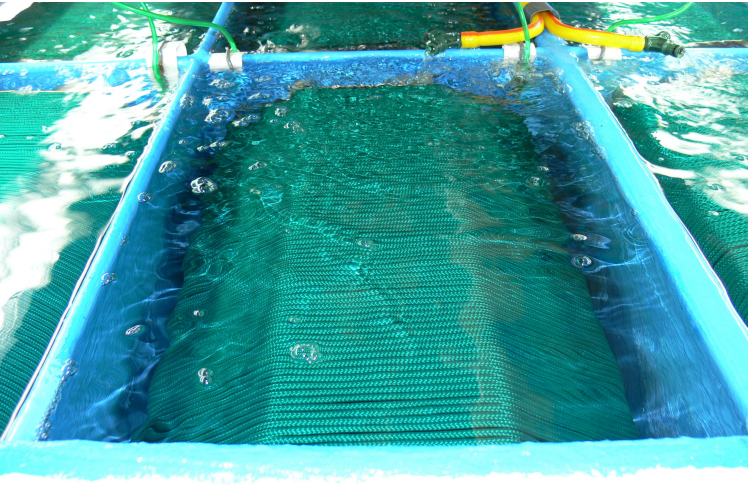


Establishment of a **fucoidan**-based value chain using endemic seaweed



- **Sustainable harvest (sampling/cultivation)**
- Controlled quality of endemic algae
- Innovative and sustainable processing
- New compound quality
- New products (cosmetics, pharma)

Development of sustainable mariculture and harvesting techniques



Leitfaden für nachhaltige marine Aquakultur

P. Krost
S. Rehm
M. Kock
L. Piker

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ecosma
Ecological Certification of
Sustainable Marine Aquaculture



Conclusion:

1. The economic **potential** of marine living resources **is tremendous**
2. Marine Biotechnology created first businesses with **minor** economical **importance** within a **low-risk** business environment
3. The **integrity of the marine ecosystem is the basis** for tapping the tremendous innovation potential
4. **Pollution and climate change** are gnawing on ocean's integrity and thereby **shrinking the innovation potential**
5. A smart **management** of the marine ecosystem and its resources is **underdeveloped**

We add value to Marine Biodiversity

