Extraction of high value ingredients from macroalgae

The Right Chemistry

Olav Gåserød and Trond Helgerud

BIOPROSP_15

Industry With a Long History in Norway

1939	AS Spesialimpregnering starts in Drammen. Production of life vests, then other products like alginate. Seaweed from Drammensfjorden and Oslofjorden
1959	AS Protan acquire the textile plant Vormedal Fabrikker in Karmøy kommune
1961	Production of alginate starts in Vormedal
1964	Mechanical harvesting of seaweed starts, without cutting from 1972
1980	Norsk Hydro AS acquires Protan Biopolymer AS
1996	Pronova Biomedical (NovaMatrix) is established
1996	Algea splits out from Pronova
1999	FMC Corporation acquires Pronova Biopolymer AS
2008	FMC Corporation acquires ISP Alginates in Girvan, Scotland
2012	Investing 70+MNOK to expand one production line in Vormedal
2013	FMC Health and Nutrition acquires EPAX in Ålesund – manufacturer of Omega-3 fish oil (1.8 BNOK)
2014	FMC announces plans to invest 500MNOK in the Vormedal plant over the next years

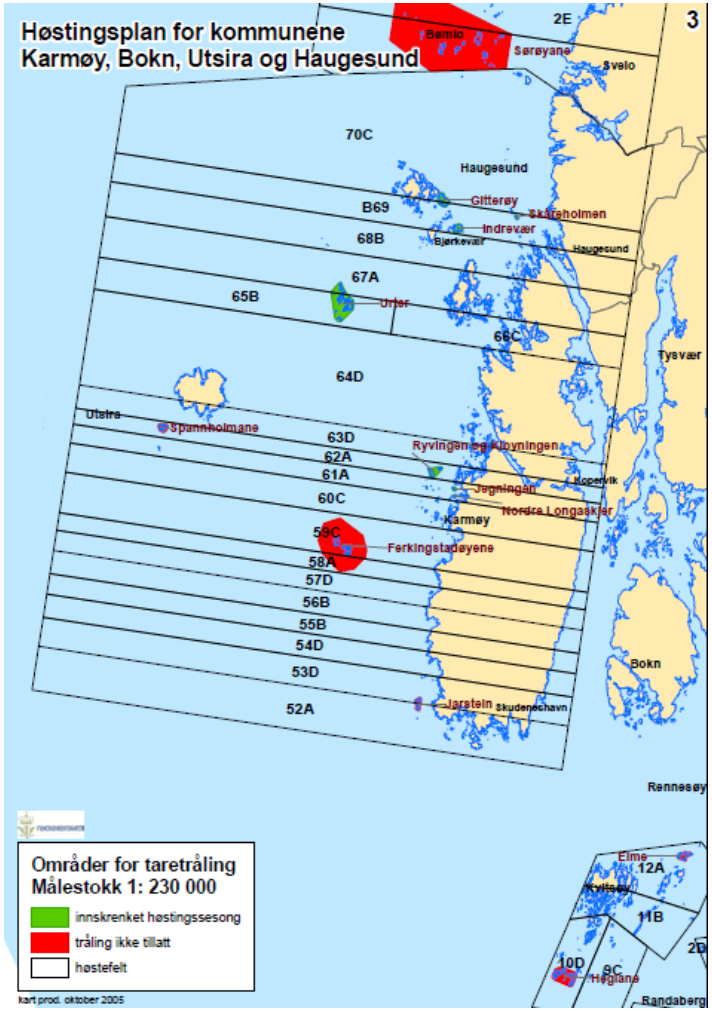
FMC BioPolymer AS - Long History of Seaweed Harvesting

- Seaweeds have been used in Norway for centuries for soil improvement, fuel, nutrition and livestock feed.
- FMC has extracted alginate since 1943. (First commercial alginate production was established by AIL in UK in 1929)

- The industry established a plan for how to harvest in a sustainable way, and during the 1970s this plan was adopted by the authorities.
- Increased alginate demand has gradually required field expansion

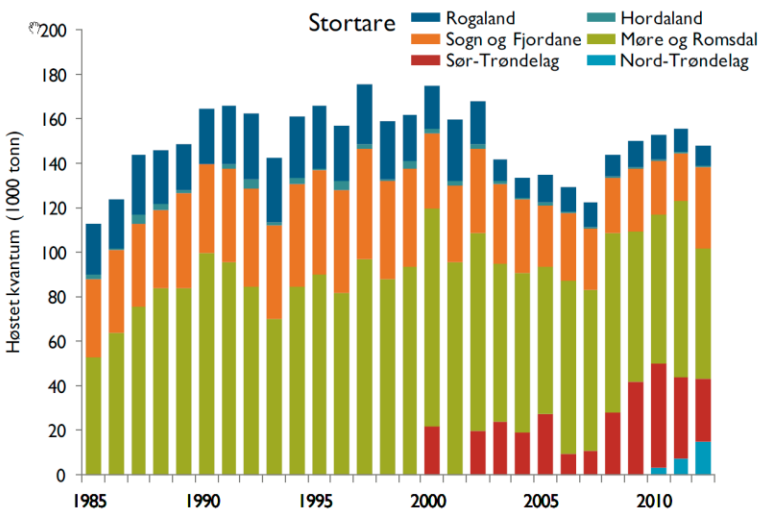
Laminaria hyperborea, a Unique Resource

- Estimated 50-60 mMT biomass at the Norwegian coast
- In the range of 7 mMT removed annually by wind and wave action
- FMC is harvesting approx 150-170.000 MT annually
- 4-5 year harvesting cycle allows regrowth of seaweed

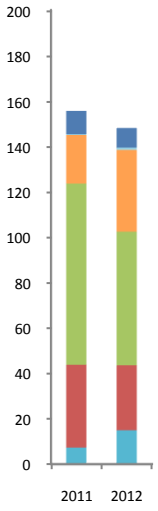


50 years of Sustainable Harvesting

- Seaweed beds are evaluated by Institute of Marine Research (IMR) to be in good and stable condition
- Stable harvesting with small variations year to year
- World class sustainable harvesting regime –
  - Other countries are looking to Norwegian systems when establishing their own
  - No overharvesting like seen in France, Chile, and Peru



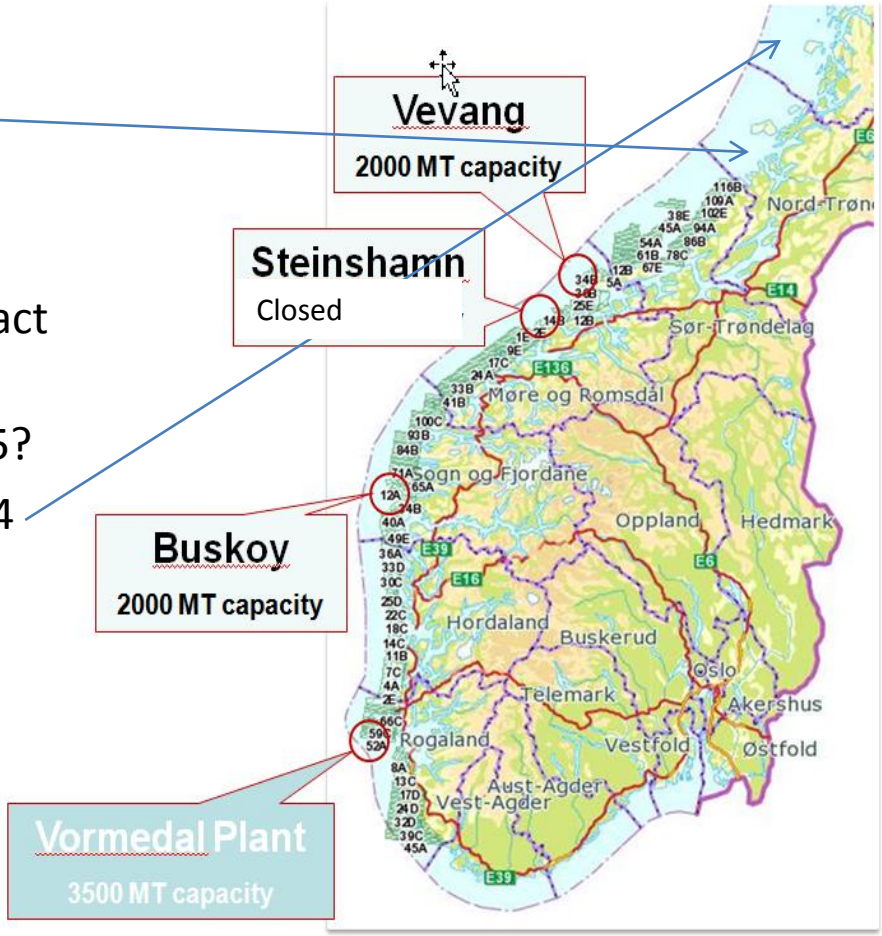
Source: Havforskningsrapporten 2013



Source: FMC

Seaweed Harvesting Future

- Each county is now responsible for regulations in their area.
- Trial harvest in Nord-Trøndelag 2010-2014
  - Up to 15,000 MT/yr during trial period
  - Rich seaweed beds
  - IMR reports no significant negative impact on marine organisms
  - Permanent harvesting permit from 2015?
- Trial harvest in southern Nordland 2013-2014
  - Up to 10,000 MT/yr during trial period
  - Applied for 2015



Being a Single, and Small, Player, Creates Some Challenges With Respect to How the Public Perceives Our Activities

Seaweed Harvesting - Myths and Facts

Myth	Fact
Negative impact on fish/ marine organisms	IMR studies in Nord-Trøndelag 2010-2014 and Nordland 2013-2014 concludes no significant negative effects of seaweed harvesting are seen on fish and other marine organisms (like crabs)
Negative influence on seabirds	Seaweed harvesting not shown to affect the availability of feed for seabirds FMC harvest close to nesting places for shag (”toppskarv”) in Rogaland. Ambio Miljørådgivning on behalf of the county authorities reports significant increase in the number of shag (1978-2006)
Increased shore erosion by wave action	Institute of Geology (UiB) : Seaweed bed effects on waves only seen at low tides and small waves (at these conditions erosion is not significant) No effect from seaweed beds during storms and huge waves, which are the conditions detrimental for constructions (like bulwarks)

Value Creation Based on a Renewable Resource

FMC’s alginate plant in Karmøy kommune

Laminaria hyperborea is a Unique Norwegian Resource

The Alginate Business Has Changed Over the Last 10 Years

- Worldwide annual production is approx 40,000MT; +2%/yr
- 40-50% of the production used in textile printing paste
- Seaweed cost has increased significantly since 2007, due to shortage and tightening regulations
- Only three Western alginate manufacturers left
- World's main manufacturing capacity located in China
- No new players in market due to very high entrance cost
- FMC consolidated the product portfolio after the acquisition of ISP Alginates in 2008, and is focusing on high quality, high value products for food and pharmaceutical applications

Going from traditional textile printing ....

.... to 3D printing of human organs

Applications of Alginate – Well Established Market, But Some Interesting Newcomers

- **Pharmaceutical**
  - Anti-reflux; treatment against gastro-esophageal reflux. Sodium alginate is the active ingredient (API)
  - Sustained release of actives from tablets
  - Wound healing; highly absorbing calcium alginate wound dressings

- **Food**
  - Stabilization of foods; e.g. Italian type ice cream, low fat spreads
  - Gelling; provide structure to foods like bakery creams, onion rings, pimiento, fruit fillings in cereal bars
  - New and creative foods - molecular gastronomy (Ferran Adria), artificial caviar, dried brown algae

- **Specialty/Industrial**
  - Personal care, water treatment, welding electrodes
  - Self-extinguishing cigarette paper

Some Examples of R&D Projects and New Products

Alginate sausage casing coextrusion process

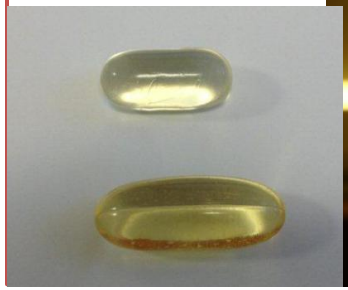
BBC NEWS

"Seaweed fights obesity, researchers in Newcastle claim"
http://news.bbc.co.uk/2/hi/uk_news/england/tyne/8579472.stm

- >1 B overweight people globally -
- Alginate can reduce lipase activity, increase fat excretion
- Alginate can provide satiety

Alginate Capsules

- New process, seamless shell
- Thinner capsule wall gives a higher effective volume
- Inherent enteric properties (no more fishy after-taste)
- Vegetable; non-animal
- Patented technology



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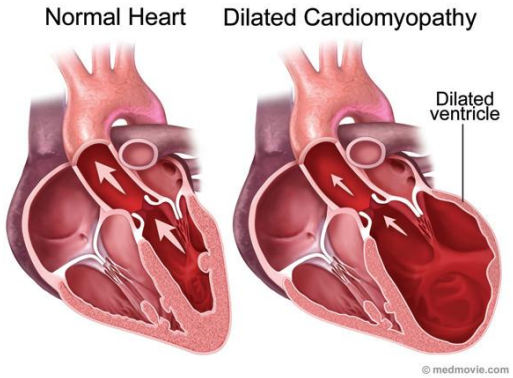
Exciting Opportunities in Biomedicine

Regeneration of bone stucture

- Alginate + demineralized bone
- Commercial product used by surgeons

Reconstruction of the heart muscle

- Alginate gel strengthen heart ventricle after infarcts
- Technology and production developed by NovaMatrix in cooperation with Folkehelsa and customer
- CE approval in 2014. Regular clinical use from 2015



Implanted liver cells encapsulated in NMX alginate

- Intermediate treatment before transplantation
- Established procedure at King's College Hospital (UK)

http://www.bbc.co.uk/news/health-15744176

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NovaMatrix™ Ultrapure Polymer Systems

Other Biomaterials from Macroalgaes

Chemical Composition of *Laminaria hyperborea*

Component	Stem [%]	Leaf [%]	Reference
Water	77-89	84-87	7,10
Ash	34.5±2.5	16-37	1, 2, 10
Alginic acid	33.4±2.8	17-34	1, 2
Laminaran	0.68±0.28	0-30	1, 2
Mannitol	5.9±2.4	4-25	1, 2
Fucoidan	2-4		8
Other carbohydrates	Traces		8
Protein	8.9±1.6	4-14	1, 2
Fat	0.63±0.14		1,2
Fibre (cellulose)	10.4±0.8		1 ,2
Polyphenols	1 (bark)		4, 5
Iodine	0.74±0.11		1, 2
K	6.3-11.0		3, 9
Na	1.6-3.0		3, 9
Ca	1.4-3.0		3, 9
Mg	0.6-0.7		3, 9
S	1.2-1.3		9
P	0.2		9

Based on dry matter

Source: S.J.Horn, PhD thesis (2000)

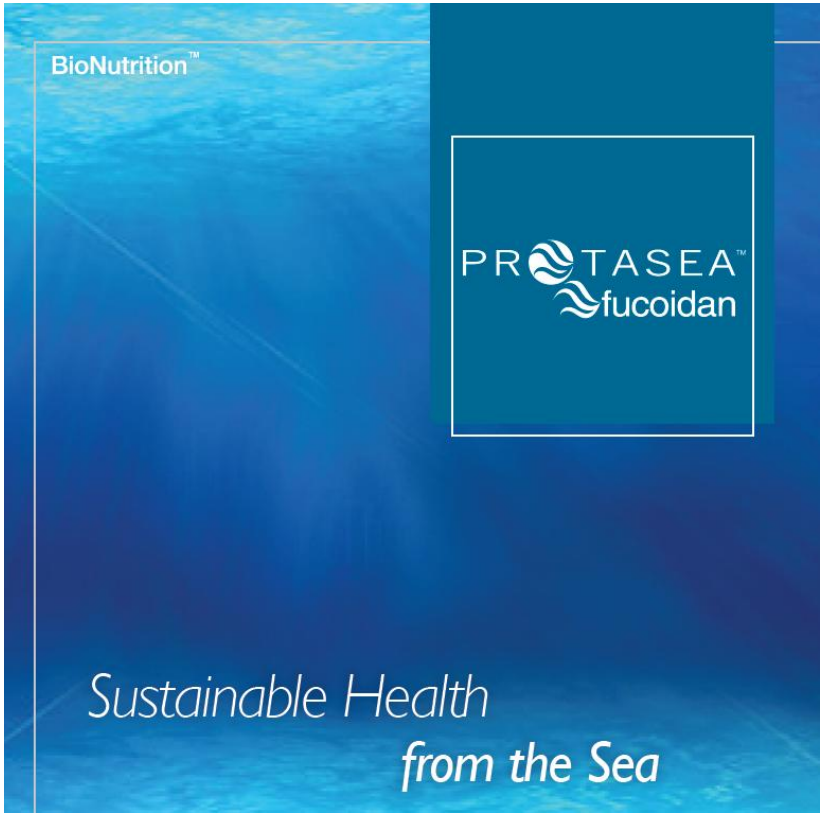
1) Haug and Jensen (1954)
2) Jensen and Haug (1956)
3) Jensen (1954)
4) Haug and Larsen (1958)
5) Ragan and Jensen (1977)
6) Larsen and Haug (1961)
7) Baardseth and Haug (1953)
8) Indergaard (1983)
9) Hanssen et al. (1987)

ProtaSea™ Fucoidan

Characteristics

- Water soluble polymer collected from fresh *L. hyperborea* stored in Haugesund.
- Large molecule, highly branched, highly sulfated
- **Bioactive properties specific to seaweed species**
- 975+ scientific fucoidan publications (PubMed) as of November 2011
- Sustainable, green, high capacity, GMP manufacturing process

Target Segment	$100M Fucoidan market in Japan/Korea
Launch:	2013 Q1
Competitive Adv.	•Efficacy, clinical data, regulatory, purity, isolation process



Competitive Advantage and Utility

- A unique, **patent pending process** for obtaining high purity fucoidan (>85%)
- **The only fucoidan with US FDA approval for supplements** – NDI approval in 2013

FMC

PROTASEA™ fucoidan

Laminaran: ß-Glucan

- Laminaran is a ß-1,3-glucan with ß-1,6-glucan branches
- Physical properties and bioactivity of beta glucans depend on branching and source
- Activation of the immune system through binding to phagocytes receptors
- Dietary fiber

Health claims

- Several claims in current products on the market, still to be better documented:
- "*Beta* Glucan is used to maintain or stimulate the effectiveness of the immune system".
- EFSA claim evaluations (2010)[1)]:
  - "Oat beta-glucan has been shown to lower/reduce blood cholesterol. Blood cholesterol lowering may reduce the risk of (coronary) heart disease." 3 g/day
  - "The Panel concludes that a cause and effect relationship has not been established between the consumption of Yestimun® and the initiation of appropriate innate and adaptive immune responses."
- Potential use in nutraceuticals/food supplements, beverages, energy bars, animal feed

Other applications:

- Commercially available for agricultural crop protection

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[1)] http://www.efsa.europa.eu/en/efsajournal/pub/1885.htm , http://www.efsa.europa.eu/en/efsajournal/pub/1607.htm

www.stortare.no