

*Advanced*  
**BIO**POLYMERS

*Health Sea Symposium  
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*"Tailored Chitosans; Structure – Function – Application"*

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# Outline

- Advanced Biopolymers AS
- Basic structure
- New and extended matrix of functionality
- Functionality
  - ❖ Physical
  - ❖ Chemical
  - ❖ Biological
- Applications

# Advanced Biopolymers AS

- History

- Established on the basis of new breakthrough technology for tailoring of chitosans. Entrepreneurs from industry (Mr. Einar Mustaparta) and university (Professor Smidsrød and Professor Vårum).

- Location

- Establishing semi-industrial plant South of Oslo (Porsgrunn) in a process and R & D cluster
- Production capacity of about 10 tonnes per year

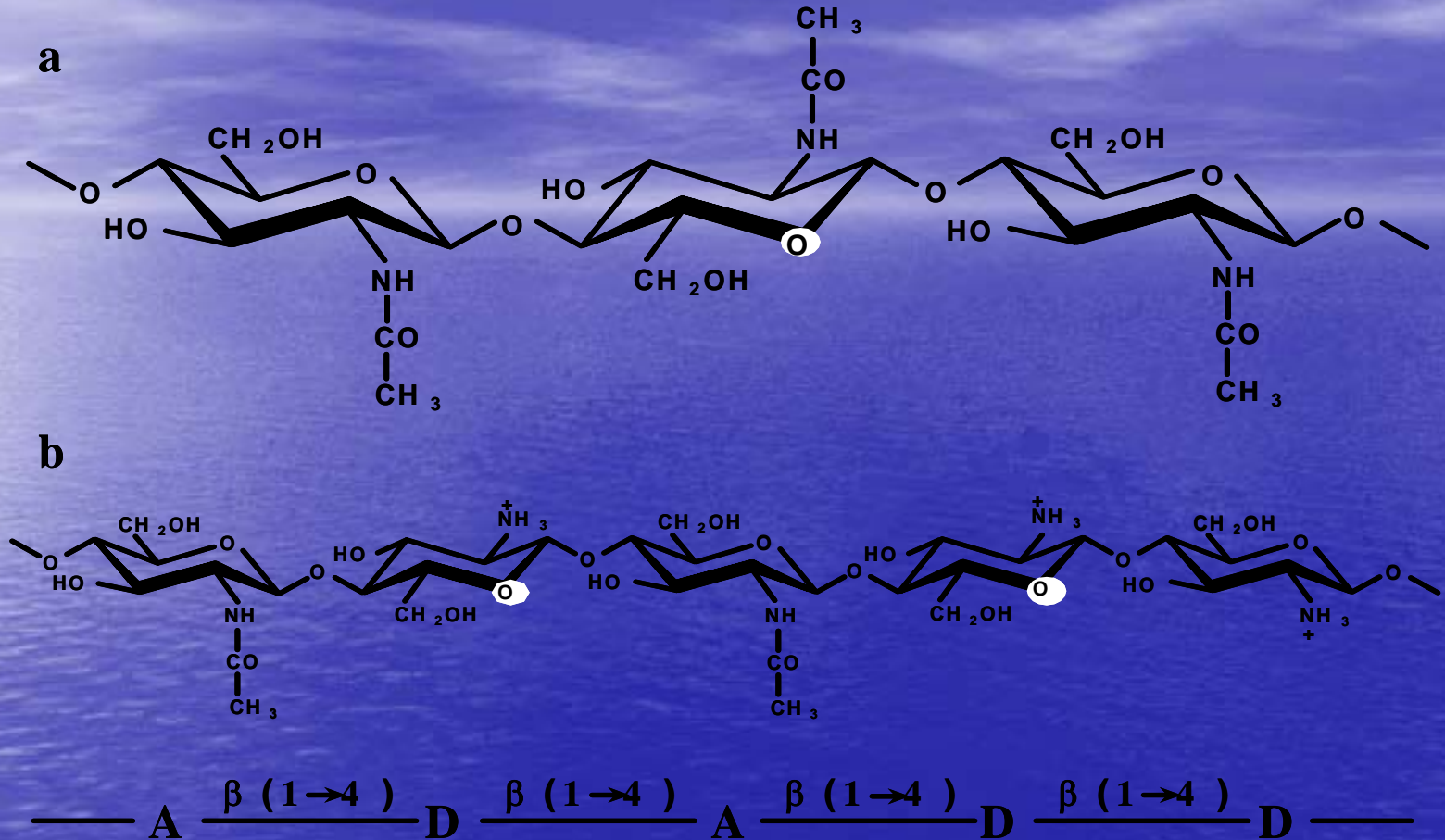
- Business idea

- Based on patented technology manufacture, develop, market and sell chitosan biopolymers with required and reproducible quality to global partners applying these as a functional ingredient in high value applications.

# We offer partners/customers

- We help to solve functional and technical challenges within *high value ingredient markets*.
- The company is based around the commercial application of chitosan biopolymers as an excipient- / semi active ingredient protected by IP
- Our background rights pave the way for product/application development with IP potential
- One segment is licensed out to a leading global ingredient company within food and beverages

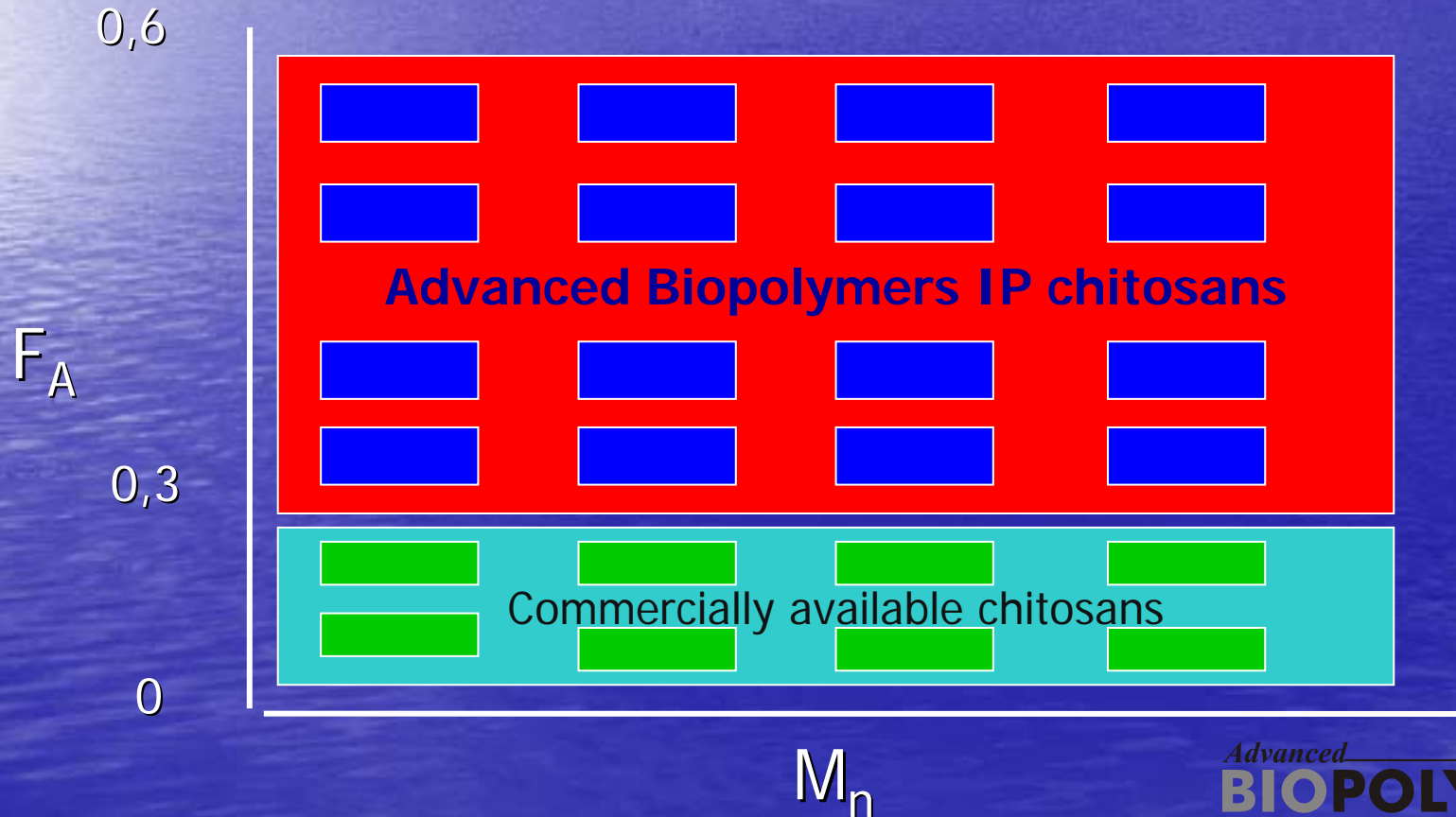
# Chitin and Chitosans



- chemical composition ( $F_A$  or  $DA$ ) and sequence of monomers along the chains
- molecular weight and molecular weight distribution

# Chitosans

## Structure – Function relationship



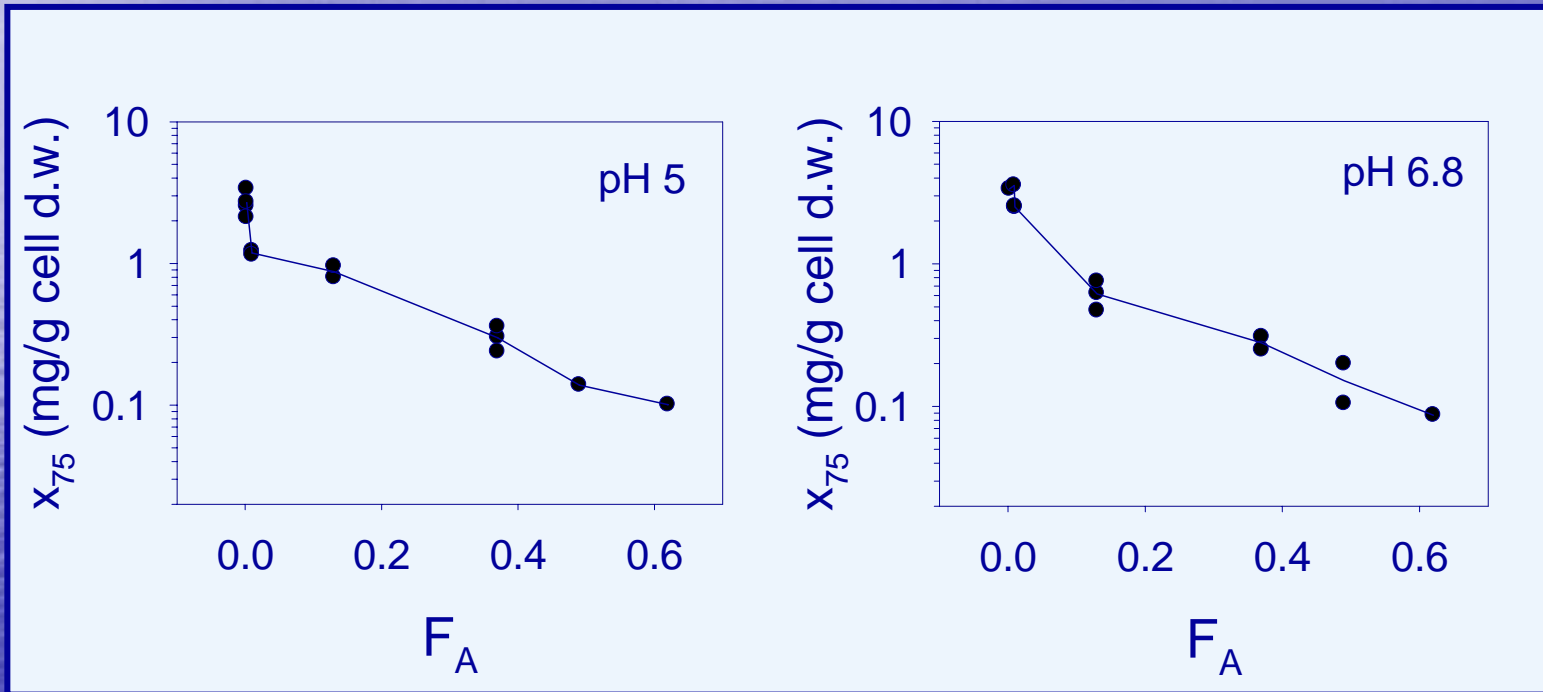
# Chitosans

## Structure – Function relationship

- Physical properties
  - Flocculation
  - Solubility and Charge Density
  - Stabilising / Emulsifying
- Chemical properties
  - Acid catalyzed Degradation
  - Stability as a function of pH and Sterilisation of Chitosan Solutions
- Biological properties
  - Enzymatic Degradation
  - Thight junction opener

# Physical properties

## Flocculation of *E. Coli* - effect of $F_A$ -



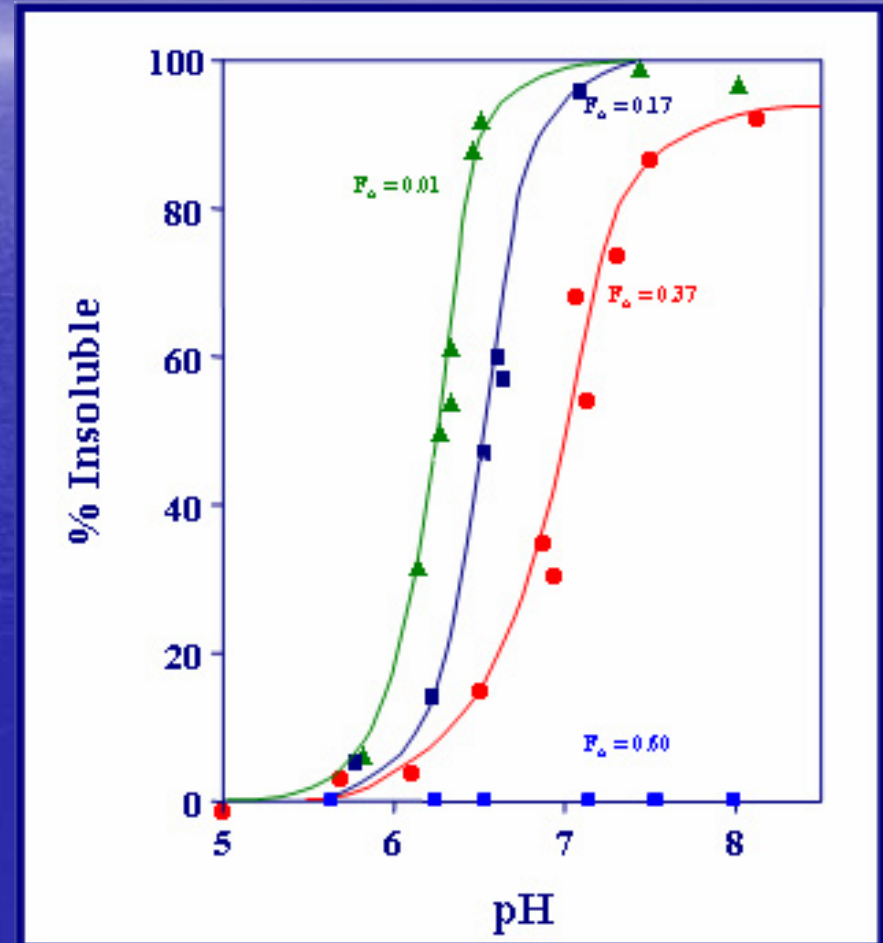
- flocculation efficiency strongly increases with increase in  $F_A$

Strand S.P. *et al.* (2001), *Biomacromolecules*, **2**, 126-133.

# Physical properties

## Solubility and charge density

- Three parameters determine solubility of chitosan in water:
  1. pH – protonisation of amino group (D-unit)
  2. Ionic strength (salting out effect) of the solvent
  3. Ions that interact with chitosans.
- Today's commercial chitosans precipitate at pH level 6 and higher
- Chitosans characterised by high  $F_A$  value (0,4-0,5) and medium  $M_n$  are neutral soluble !



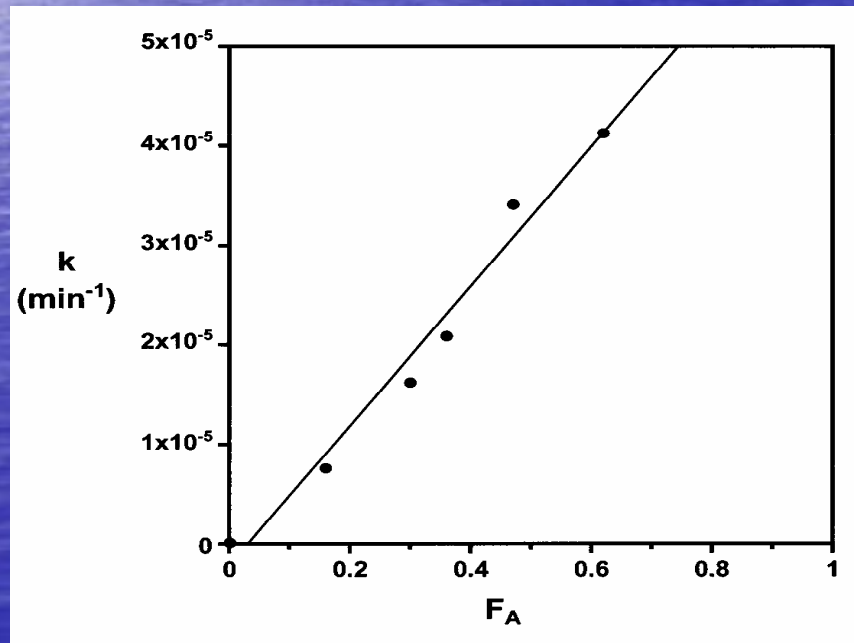
# Physical properties Emulsifier - stabiliser

- Amphiphilic polymer
  - ❖ The possibility for adjusting ratio A-units/D-unit
  - ❖ Emulsifying effects
  - ❖ Stabilising effects in emulsions

# Chemical properties

## Acid catalysed degradation

- Initial Acid catalyzed degradation rate constant is proportionate to  $F_A$
- A-A and A-D glycosidic linkage was found to be hydrolyzed with about three orders of magnitude higher rate than D-D and D-A (Vårum et al. 2001)

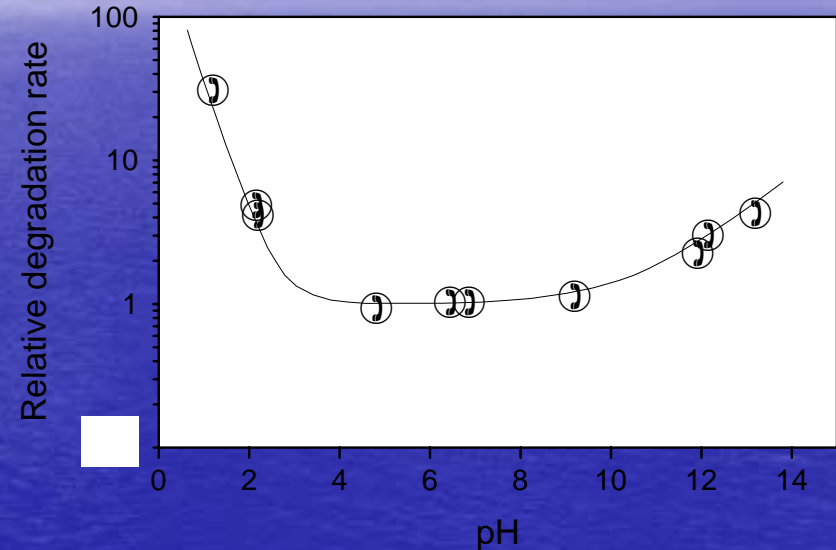


Vårum & Smidsroed, 2004

# Chemical properties

## Stability – f(pH) and sterilisation -

- pH dependent stability
  - High rate below pH3 and over pH11
  - Stable around neutral



- Sterilisation by autoclaving (120 ° C for 20 min) without severe degradation
  - At pH 4,5;  $F_A 0.01 < F_A 0.35 < F_A 0.60$

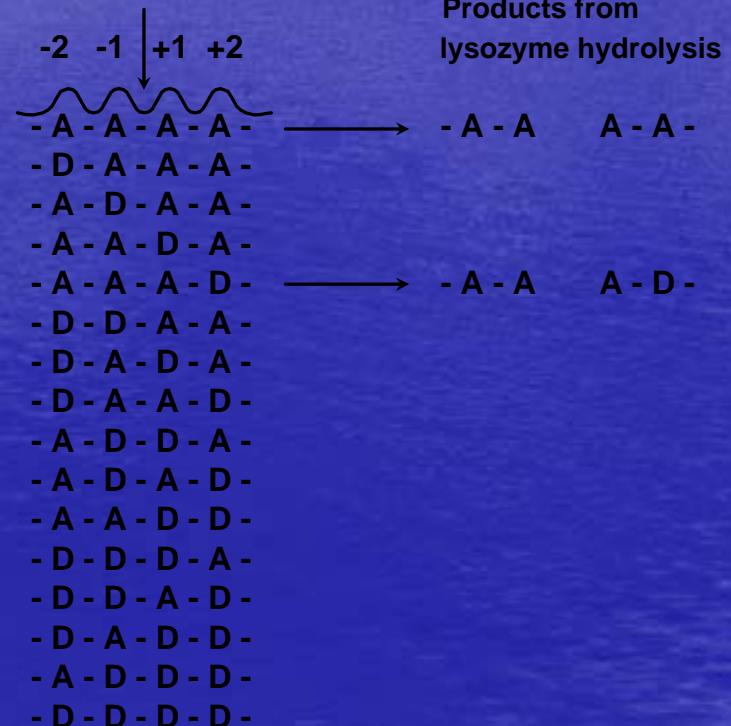
Vårum & Smidsroed, 2004

# Biological properties

## Enzymatic degradation

- Lysozyme hydrolyze chitin and chitosans*
  - Degradation rate highly dependent on  $F_A$  (ie. proportionate to  $(F_A)^4$ )*
  - A minimum of four A units to obtain maximum degradation*
  - Makes it possible to tailor chitosans with predetermined degradation rate for use on/in the human body*

### LYSOZYME SUBSITES



# Biological properties Delivery / release systems

- Bioadhesion and biodegradability
- Facilitating opening of tight junction (epithelial cell layer)
  - ❖ Holme et. al. 2000 - Caco-2 cell system
  - ❖ Chitosan with a  $F_A$  of 0 – 0.40 and  $M_n > 100$  kD increased the permeability of human intestinal epithelial cells.
- Reversibility of the opening function is highly dependent of a balance between  $F_A$  and  $M_n$ .

# Potential Applications

- Food system
- Personal care system
- Biomedical system

# Food application

- Taking advantage of the amphiphilic character
  - Adjusting ratio H-fobic/H-philic to food system requirement
  - Molecular weight and/or concentration in order to achieve stabilising effect.
  - pH and heat stable within certain intervals
- Emulsifier & Stabiliser in one single substance

# Personal Care Skin Care Application System

- Deliver active agents to skin cellular layer
  - Anti microbial topological effect
  - Chitosan tight junction opener
  - Tailored biodegradability (ie. Opening effect substituted by oligo – and/or monomer effect on skin)
- Product-technology effect
  - ❖ emulsifying – stabilising function

# Biomedical Application

## Nasal delivery

1. Bioadhesion when exposed to mucosa surface
2. Opening of epithelial tight junction and delivery of active drug to plasma
3. Biological degraded by lysozyme and thereby terminating polymer effect.

# Conclusions

- Functionality is dependent both on FA and Mn.
- New potential for development of applications when extending the axis of FA from 0,3 to 0,6
- Advanced Biopolymers IP (pending) technology is first to market with a reproducible quality of high FA chitosans