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Cow's milk protein hydrolysates

Using technology to improve allergy management

Els van Hoffen els.vanhoffen@nizo.com
AgriFood Top 01-06-2016

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First choice of nutrition for infants: Breast milk

Nutrients in breast milk

- Proteins: whey > casein
- Fats: Essential fatty acids, polyunsaturated fatty acids
- Carbohydrates: mainly lactose
- Minerals, vitamins, trace elements

Immune-related components and growth factors

- Antibodies
- Bioactive cytokines (TGF- β , IL-10)
- Oligosaccharides
- Hormones

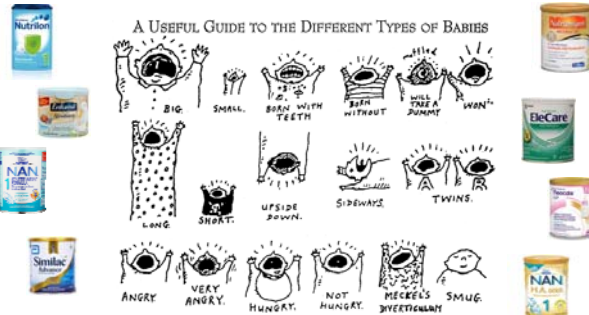


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If breast milk is not available: Infant formula

A USEFUL GUIDE TO THE DIFFERENT TYPES OF BABIES




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Types of infant formula

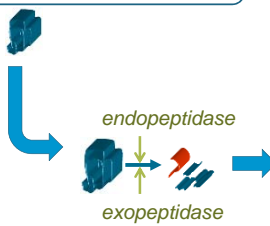
- Intact protein: casein > whey
- Hydrolysed protein: casein or whey
 - Partial hydrolysate: no size-filtration
 - Extensive hydrolysate: peptides (e.g. <1500 Da)
- Amino acids



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Why applying protein hydrolysis?

Process	Benefit
Protein + process conditions	Amino acid production Improving protein extraction Increasing protein solubility
	Debittering Improve flavour
	Reducing allergenicity Bioactive peptides production
	Tailoring texture


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Hydrolysed formula in cow's milk allergy (CMA)

Adverse reactions to cow's milk

- Cow's milk allergy
 - Immune disorder
 - Reaction to milk proteins
- Cow's milk intolerance
 - e.g. Lactose intolerance
 - Deficiency in β -galactosidase



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Hydrolysed formula in CMA

Reduction of symptoms



American Academy of Pediatrics - Committee on Nutrition

Hypoallergenic:

- Tested in infants with hypersensitivity to cow's milk
- Properly conducted elimination-challenge tests
- No reaction in $\geq 90\%$ of infants

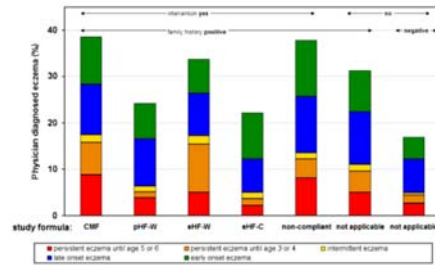
→ Extensive hydrolysates or amino acid-based formula are effective

Hydrolysed formula in CMA

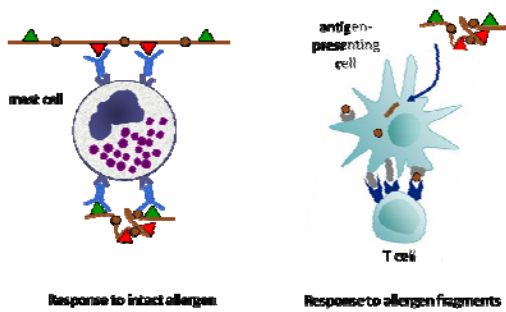
Prevention of allergy



Development of tolerance to food requires exposure
GINI study: prevention of eczema in children at risk



Allergic response



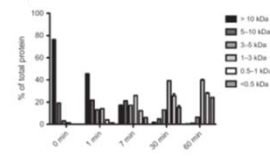
Hydrolysed formula in CMA

Prevention of allergy

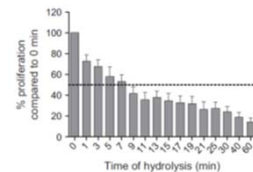


Effect of hydrolysis on T cell response
T cells from CMA patients

Distribution of fragment lengths



Impact on T cell response



Hydrolysed formula in CMA

Prevention of allergy



Preventive treatment with partial whey hydrolysate
Prevention of CMA in a mouse model

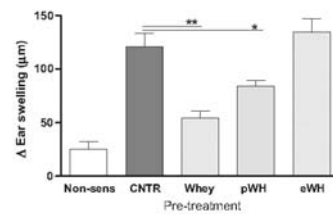


Hydrolysed formula in CMA

Prevention of allergy



Preventive treatment with partial whey hydrolysate
Prevention of CMA in a mouse model



Characterization and targeted production of hydrolysates

Better characterization of hydrolysates

- Size distribution
- Peptide profile
- Potential bioactivity

Targeted production

- Know which peptides are important
- Better understand the hydrolysis process

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13

Enzyme selection pipeline

The pipeline consists of the following stages:

- >25 million scientific articles -> Data Mining**: Utilizes unique proprietary bio-IT tools.
- Expert advice for selecting enzymes**: Involves commercial enzymes or enzyme discovery.
- HTS analysis (2mL)**: High-throughput screening (<5000 conditions) robot & automated analysis.
- Optimization of conditions (200mL-10L)**: Screen up to 12 conditions per day to optimize process.
- Product (200L - 2m³)**: Food grade pilot-scale hydrolysis and downstream processing facilities.

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14

Data mining

The Venn diagram includes:

- Machine Learning**
- Statistics & Modelling**
- Data Analytics**
- Food & Processing Domain Expertise**
- Machine Learning**
- Machine Learning**

Other components include:

- Biological analysis**: Shows chromatograms and spectra.
- Quality control**: Shows a flowchart of the process.
- Comparative analysis**: Shows a scatter plot of Mead Johnson products.
- Functional analysis**: Shows the NIZO BioActivity Database.

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Characterization of hydrolysates

Peptide profiling

4 extensive hydrolysates

Lambers et al. Food Sci Nutr 2015;3:81-90

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Characterization of hydrolysates

Clustering analysis

The scatter plot shows differentiation factors 1 and 2 for various companies. The dendrogram shows the hierarchical clustering of hydrolysates based on their peptide profiles.

Lambers et al. Food Sci Nutr 2015;3:81-90

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Cow's milk derived peptides

Treatment of allergy

Oral immunotherapy using whey peptides

Treatment of CMA in a mouse model

The flowchart shows the experimental timeline: Induction of cow's milk allergy (0-28 days), Oral immunotherapy (28-84 days), and Analyse allergic response (84 days).

Meulenbroek et al. Pediatr Allergy Immunol 2013;24:656-64

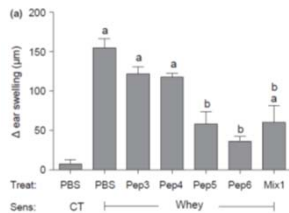
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18

Cow's milk derived peptides Treatment of allergy



Oral immunotherapy using whey peptides
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Meulenbroek et al. *Pediatr Allergy Immunol* 2013;24:656-64

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19

Conclusions



Use of hydrolysates for treatment/prevention of CMA:

- Extensive hydrolysates are adequate for reduction of symptoms in CMA
- Hydrolysates may be effective in prevention of CMA or eczema

→ Mechanism of action: Immune tolerance? Other bioactivity?

→ Better characterization → targeted production and application of protein hydrolysates

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20

Acknowledgements



NIZO food research

Hans Kusters
Thom Huppertz
Wynand Alkema

Nutricia Research

Laura Meulenbroek
Leon Knippels
Johan Garssen



UMC Utrecht

Stans den Hartog Jager
Carla Buijnzeel-Koomen
André Knulst
Edward Knol



Mead Johnson

Tim Lambers
Ric van Tol



UMC St. Radboud

Jolijn Gloerich



UIPS

Betty Lobato – van Esch
Linette Willemsen



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21