NIZO Vision

№ 5 A news publication of NIZO food research

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Functional food

The development of mankind has brought our society great improvements in technology, wealth, and health. People may expect to live considerably longer than a few centuries ago, thanks largely to food technology and life sciences. And the food we eat is safer than ever before. Compared to the diet of early man, however, the diversity of food and the variety of nutrients has actually reduced. Bad components may have been removed, but have all beneficial ingredients been retained? In an era when many human ailments are linked to our way of life and increased life expectancy, people look increasingly towards their food in order to stay healthy.

The first place where food begins to impact our health is the gut, which receives about 60 tons of food in a human lifetime. The gastro-intestinal tract is exposed to many healthy, but also many unhealthy effects from food. The gut's surface (between 250 and 400 m2) is its main organ. It determines the secretion of lubricants to control the passage of food, and it controls the release of digestive enzymes, the absorption of food components into the bloodstream, resistance to infections, and more. Our health depends greatly on its performance, and that is why NIZO food research has chosen to focus its nutritional expertise in this area.

Functional foods are expected to increase the quality of life by preventing and/or postponing the onset of diseases. For them to be accepted, it is essential that their function be proven! This requires knowledge of the mechanisms involved and measurement of the right biomarkers to demonstrate effects. Human trials are also required to deliver proof for the responsible positioning of foods. Moreover, the food industry needs ways of maintaining the functionality of ingredients during processing and shelf life.

In this issue, we illustrate aspects of our involvement in the process of functional food design. This involves co-operation with other researchers, with industry, and governments. With its combination of nutritional expertise and ability to optimise food composition and food processing, NIZO aims to help industry to formulate new reliable functional food products.

Dr. Ad Juriaanse, Managing Director
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Column

Consumers all over the world have shown to be highly interested and receptive to foods with health benefits. Projections on sales have led to a boost in the industry producing health-promoting ingredients. "The focus on new products increasingly shifts from nutritional value towards health claims regarding what the product can do for you," agrees Marian Geluk, sales manager, and Hans Snel, project leader nutrition at NIZO food research. To increase the confidence of the consumer in functional foods, it is of utmost importance to support new products with valid health claims. "In that light, we should understand and anticipate the activities of the European Commission who prepare a regulation on nutritional, functional and health claims made on foods," says Marian.

Ir. Marian Geluk, Sales Manager

Healthy business in functional foods

Leading role

NIZO food research has a long history in supporting the industry with the development of health claims. The link between the profound knowledge of lactic acid bacteria and probiotics is easily made, but it goes much further. "NIZO plays a leading role in the areas of colon cancer prevention and resistance to infections," explains Hans. "We were the first to explain how calcium from milk can protect against colon cancer. Later, we found out that calcium —by using the same mechanism— could also help to fight salmonella infections. You see, this mineral does more than building bones." New health studies at NIZO analyse gene expression in the gut wall to find the molecular basis of these effects. In other studies, food ingredients have been found that protect against infectious diseases such as Influenza. "Using a strong focus on the working mechanism, our investigations have provided companies not only with important data, but frequently also with unexpected new concepts for future products," continues Marian. "In other cases, unravelling the working mechanism by animal or in vitro experiments, has led to the right biomarkers to verify the findings in humans."

"Gut health and resistance to infections are key nutritional areas for NIZO food research," remarks Marian. "But we focus in our work not only on the intestinal tract. We make sure that our expertise utilises the synergy with other NIZO expertise areas like microbiology (lactic acid bacteria), product design (encapsulation) and manufacturing. This ensures top science in combination with applicability." ▶

Dr. Hans Snel, Project Leader Nutrition

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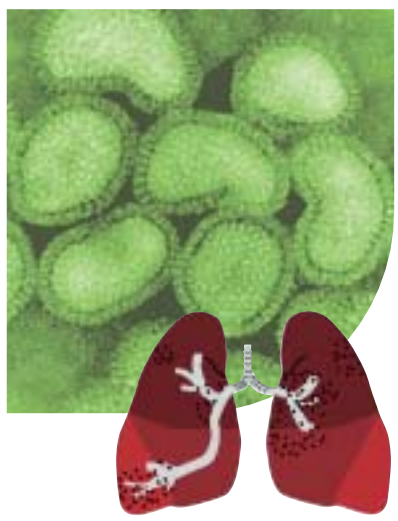
Interview



One of the factors determining our resistance against infections is our food. Consumer research has confirmed that people understand this role of food and are prepared to change their diet if they need to boost their resistance. The influenza virus is among the most common pathogens that infect humans. Functional food ingredients can be perfect carriers for immune enhancers.

Eating to cure the flu

For manufacturers of food ingredients, researchers at NIZO food research have recently developed a rat infection model in which the effect of subtle changes in the diet on resistance to the Influenza virus can really be measured.

Based on information on ingredients, the influenza studies can be designed such that the mechanism underlying the health benefit can often be clarified. This biomarker developed by NIZO provides a powerful extrapolation model for human trials and the need for large epidemiological studies (and high costs) can thus be reduced. Some of the advantages of the model are:

- the Influenza virus is administered through the nose
- the pathogen causes a transient infection, analogous to that in humans
- the animals survive the infection and thus both short and long term effects can be studied

Companies can build on this knowledge and extend the work to human trials to prove that ingredients can really fight the flu. The first food ingredients have been identified that were effective in clearing the virus from the lungs of rats by improving the immune reactivity.

By studying the same immune parameters it is possible to establish effects also in humans. In combination with animal studies this builds a strong case. Truly functional foods against the flu are within reach!

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NIZO food research

Interview

Jan Steijns, Head of the Campina 'Centre of Expertise Nutrition' (CoEN)

In a world that's more demanding of it's citizens than ever, health has become an important item for food products. With the new slogan, 'It's in our nature', Campina responds well to this development. In the last years the major Dutch producer of dairy products has introduced the 'health brand' Vifit, with some remarkably successful products. At the base of these health products stands scientific research that is mostly conducted by a special team, at Campina's facilities in Wageningen.

In search of the goodies from milk

One of the successful products that have been marketed under the Vifit label is Optimel, a yoghurt or yoghurt-drink that contains zero % fat. Other products are Calcimel, with extra calcium, and Vitamel, with extra vitamins and the probiotic LGG. As the head of the Campina 'Centre of Expertise Nutrition' (CoEN) in Wageningen Mr Jan Steijns is largely involved with these and other products that are marketed in The Netherlands and in other countries. "Part of our job is to work on new product concepts together with our marketing departments", says Mr Steijns. Despite extensive dairy-research in the past, there is still a lot of open terrain left, to Mr. Steijns. "It is true that we know a lot about the composition of milk, but when it comes to the properties of individual ingredients we are learning something new almost every day, for example about a protein like lactoferrin, or about the properties of calcium."

Valuable research partner

According to Mr Steijns recent research on calcium reveals that this mineral does not only strengthen human bones, but it also attributes to a higher resistance against diseases. Furthermore it provides some protection against cancer of the large intestine. "Calcium even seems to stimulate the loss of bodyweight", says Mr Steijns. "So you see that this research can provide valuable new arguments in the marketing mix of a product like Calcimel."

Apart from nutritional consultancy the CoEN also carries out experimental research, which is done with the help of NIZO food research. Mr Steijns considers NIZO to be a valuable research partner. "NIZO food research carries out experimental animal research for us. They have very good, internationally renowned scientists to whom we also gladly turn for their advice."

What will the future bring?

"Current research reveals that the wide-spread belief that milk fat is not good for you needs reevaluation", says Mr.Steijns. "There are promising data on e.g. anti-carcinogenic properties of CLA and sphingolipids. Perhaps even more are the bioactive peptides contained in the milk proteins, which may be involved in e.g. mineral absorption, satiety regulation or blood pressure reduction. They may be released from the proteins with enzymes or produced during fermentation. However, there are still many questions to be answered. No doubt, NIZO food research can assist us here as well!"

So what should we consider him to be, scientist or marketer? "Both I guess", he smiles. "Of course I strive for the respect of fellow scientists, but the greatest joy to me comes from the observation that our product is a hit on the supermarket shelves."

Milk fat against gut infection

Milk provides us with high nutritional value. This has been known for years. Recent research at NIZO food research proves that milk may also protect you from gut infections. Digestion of milk fat releases several compounds that kills harmful bugs like Listeria and Campylobacter. Especially mediumchain fatty acids and sphingolipids, characteristic for milk fat, may be helpful in preventing diarrhoea caused by foodborne pathogens.

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See you at the Hi

NIZO food research will be present at the Health Ingredients Europe (Hi) exhibition in Paris, 17-19 September.

This year once again, a paper from NIZO has been selected for presentation during the Hi Summit. On 18 September, Dr. de Ruiter will present a paper on innovative upstream and downstream processing of health ingredients. You are invited to discuss your plans with him.

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Genomics is a hot topic in the scientific and industrial arena. It provides highly promising spin-offs for the food and pharma industries. The Dutch government, being aware of the relevance of genomics, will invest 190 million Euros in genomics research aiming to place the Netherlands in the world top league.

High stakes for genomics research at NIZO

Kluyver Centre

Together with its partners, NIZO food research has established the "Kluyver Centre for Genomics of Industrial Fermentation". In this centre, research organisations cooperate in with the fermentation industry to develop genomics-based technologies for innovations in the industry. The Kluyver Centre has already been nominated for funding! As one of four out of eleven centres, the Kluyver Centre was invited to submit a business plan for this initiative.

Nominated for funding

The Centre's output will have a decisive industrial impact by applying genomics in the following instances:
a) as a diagnostic tool for monitoring, design and optimisation of fermentation processes,
b) for efficient knowledge based development of novel industrial cultures without the application of recombinant DNA technology, and
c) for the development of highly efficient cell factories for production of flavours, ingredients and protein pharmaceuticals.

Centre for Human Nutrigenomics

In parallel with the Kluyver initiative for industrial fermentation, NIZO participates in the Centre for Human Nutrigenomics, led by Prof. Dr. F. Kok of the WUR. This centre encompasses the major Dutch universities and applied nutrition research organisations. The centre will focus on determining the relationship between food components and human gene function for healthier and safer foods.

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Continuation of cover story Healthy business in functional foods

How to create a healthy business cost structure?

When the industry succeeds in producing reliable functional foods, the consumer will be willing to pay the added value. Nonetheless, one needs to be cost effective in the substantiation of claims. "A very careful selection of evidence that needs to be gathered is critical," says Marian. "We assist companies also in this process by providing literature reviews on the current scientific knowledge," continues Hans. Developing a cost-effective production process for health ingredients is another area where huge gains can be made. NIZO food research has assisted several of its clients in designing food-grade, semi-industrial production processes.

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Urgent need for hypo-allergenic foods

Food allergies increasingly affect our lives. Many infants suffer from allergenic substances present in products containing wheat, peanuts, cows milk, or soy proteins.

Health research at NIZO food research has now resulted in a technology to selectively remove the allergy inducing peptides from cow's milk. The patented technology developed by NIZO is based on selective hydrolysis followed by down stream processing to remove the undesired substances. During in-vitro testing with human serae, no allergenic activity has been found!

With the recent US and EU proposals for labelling allergy inducing proteins, this technology offers interesting opportunities for the food industry, particularly for products like soy and wheat proteins. Currently, based on both protein hydrolysis and immunology expertise, NIZO food research is developing technologies for the production of special food peptides that may induce tolerance. This novel approach can even lead to a prevention of the development of food allergy in adults!

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What is in your guts?

In supporting nutritional claims a rapid overview of the intestinal micro-flora is needed to provide insight into, e.g., the survival of pre- and probiotics in the gut. DNA-based methods used at NIZO food research, including real-time PCR, enable rapid and specific detection and quantification of micro-organisms.

Conventional methods rely on the growth of micro-organisms on agar media and biochemical characterisation of isolates, and usually do not meet the requirements of the food industry. The proposed method has already proven its worth in the evaluation of the effect of functional food ingredients on pathogenic organisms, such as *Campylobacter* and *Salmonella*.

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New logo and house style

Over the past years, NIZO food research has widened its scope from dairy to food in its widest sense. To convey our identity as a professional contract research organisation for the food industry, the logo of NIZO food research has been modified and a house style established. This symbolises the professionalism and creativeness of our workforce and helps us to present ourselves in a uniform and recognisable way to our customers.

From now on, our new logo and house style elements will appear on all our printed and electronic information bearers.

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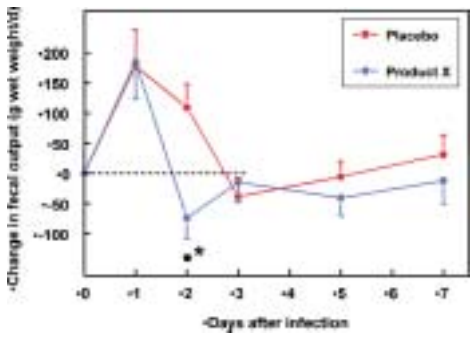
Many people suffer from intestinal infections caused, a.o., by E.coli. It would be very interesting for the industry to be able to produce foods that are not only E.coli free, but also actively suppress colonisation in the gut. With a new human infection model, NIZO recently demonstrated that dietary calcium improves resistance to intestinal infections.

Functional food improves human resistance to intestinal infection

The human infection experiment

An important claim is improvement of resistance against intestinal infections. After testing with animals, the ultimate proof that a nutrient improves human resistance to gut infections can only be obtained from human infection experiments. Obviously, infection experiments with humans are difficult to perform, but NIZO managed to overcome the problems. NIZO is involved in a long-term project on the effects of diet on gut infections, as part of the WCFS Nutrition and Health Programme. The inhibiting effect of dietary calcium on human diarrhoea was recently shown with a new model developed by NIZO in which healthy male volunteers were infected with a modified *Escherichia coli* (ETEC) vaccine, inducing mild, short-lived symptoms. This infection is relevant, as it is the main cause of traveller's diarrhoea. The results of the study were convincing: participants consuming the calcium-supplemented products had significantly less diarrhoea.



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Using Genomics to find new probiotics

Today, food and health shops stock an increasing variety of probiotic products. Health companies that develop, market and commercialise these, often well-protected strains, benefit from important competitive advantages. These companies face the challenge of accelerating product development and bringing protected and proven products to their customers.

The genomics technology has opened new avenues to accelerate product development and NIZO food research has exploited this new technology to discover unique bacterial genes that are involved in health benefits. The genetic data of natural strains are compared to genome sequence information from known probiotics, e.g., *lactic-acid* bacteria. This opens the way to screen new strains of *lactic-acid* bacteria with targeted functionality for application in food products, such as yoghurts, baby foods, or fruit juices.

In vivo experiments have led to the identification of a large number of genes that are related to survival in the GI tract. These data are now available at NIZO food research and can be used for the development of new products.

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Interview

Prof. Dr. Martijn Katan, Scientific Director of the Program on Nutrition and Health of Wageningen Centre for Food Sciences (WCFS).

"One of the most exciting discoveries over the last 25 years is the fact that folic acid prevents neural tube defects. And we expect even more of this vitamin," says Prof. Dr. Martijn Katan, Scientific Director of the Program on Nutrition and Health of Wageningen Centre for Food Sciences (WCFS).

WCFS: fundamental research for innovations in the future

Based on a joint initiative of the Dutch food industry and the Dutch government, WCFS embodies a structural co-operation between seven food companies and four Dutch research organisations. Participants join forces to accelerate fundamental and precompetitive research in areas of shared interest: nutrition and health, food texture and food biotechnology. In all these fields NIZO employees are active.

Applicable

The nutrition and health programme is focused on the nutritional prevention of health problems, including cardiovascular diseases, colon cancer and infections. "We develop biomarkers that show the effects of food components on human health, such as indicators of mechanisms -how a food component behaves on the molecular level - and indicators for health or disease," illustrates Katan.

Frontline

The nutrition program should be proud of the results it has achieved in its first four years. In the meantime, it has 75 international publications and two patents to its name, and has set up both novel mechanistic research and long-term trials in humans. At the moment, there is a three-year trial going on with 850 participants, measuring the effects of folic acid consumption on the carotid artery wall thickness. "With this trial we expect to be at the frontline of folic acid research," says Katan.

No less important, WCFS researchers at NIZO food research and Rikilt have discovered a gene that could be involved in the development of colon cancer and that is influenced by nutrition. "This finding has opened the door to genomics in food research."

The formula, by which science and industry jointly develop research, has been surprisingly successful. "Before I took up the job, I was worried that the 'short-term' money might chase out the 'long-term' money, but WCFS has proved to be capable of high-quality, long-term research." The long-term focus is one of NIZO's strengths. "In spite of its commercial approach, NIZO has kept its long-term research in both nutrition and food technology, and realises that your ideas for applied research will dry up without fundamental research," he adds.

Cross-fertilisation

Katan is enthusiastic about the cross-fertilisation within WCFS. "The molecular approach of the NIZO nutrition group has helped our group at the university to think not only of effects in humans, but also about the mechanisms behind those effects. Furthermore NIZO is now better able to translate fundamental research into human trials. For example, it has developed a method to test the infection inhibition effects of food products in humans. For the industry, this combination of mechanistic research and human trials is essential."

According to the scientific director, WCFS will increasingly focus on 'mechanistic' research and genomics. "I expect genetic susceptibility to be more important in medicine than in food. In my opinion the much-discussed personal diets will not become reality, as the number of genetic variants with a large impact on the effect of diet on health is probably small. Just like the number of people carrying these variants. However, we need research to demonstrate these facts."

High expectations

Katan has high expectations of the qualities of folic acid. "There are substantial positive effects in the prevention of cardiovascular diseases, colon cancer and perhaps mental disorders, such as Alzheimer's. We hope our ongoing trial will demonstrate some of these effects."

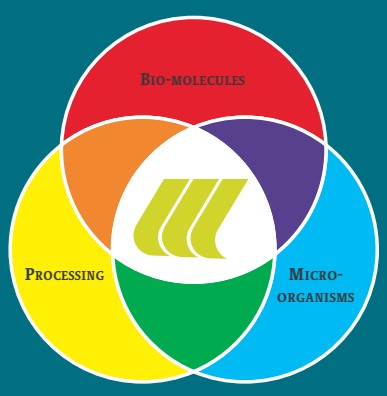
Products & Services

NIZO food research's leading areas of expertise:

Bio-molecules
- *Texture and stability*
- *Emulsions*
- *Enzymatic modification*
- *Analysis*

Processing
- *Predictive modelling*
- *Separation and drying*
- *Fermentation and inactivation*
- *Pilot plant*

Micro-organisms
- *Flavour*
- *Food Safety*
- *Metabolic engineering*
- *Health*
- *Culture collection*



Folate – a vitamin in the spotlight

Folate is an important natural vitamin that generates much interest because of its potential to reduce the risk of major illnesses of the Western world. This has led to discussions on mandatory fortification of food products, like cereals, with folic acid. NIZO food research has wide experience with fermentations and producing folates.
In collaboration with Leatherhead Food RA, NIZO also organises a training course in Ede. The course (2nd October) addresses all major aspects of folates relevant for the food industry. From function and bioavailability, to methods and current legislation.

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NIZO and its networks

Among the many networks in which NIZO participates, one has taken a unique dimension, as illustrated in the interview with Prof. Katan. NIZO is very pleased to contribute to this partnership. Sharing projects in WCFS provides critical mass for expertise and creates an excellent platform for developing new and exciting ideas!

In principle all results get published in the open literature, but of course the partners have the first right to file patents based on the findings within WCFS.

Another network in which NIZO participates is the Kluyver Centre for Genomics of Industrial Fermentation. This partnership allows fast development of genomics-based technologies for innovations in the industry.

These, and the centre for human nutrigenomics as well as many EU consortia are some of the good examples of valuable partnerships. They fit perfectly in NIZO's long tradition of combining excellent science with a high relevance to industry!

Pilot plant facilitates human health trials

When the Human Biology Department of Maastricht University needed a product with a specific fatty-acid composition for their health studies in humans, they didn't have to look far. At NIZO's pilot plant, margarines and cheeses can be produced with unusual fats. "For our human trials, we often need foods with a special composition," says Prof.Dr.Ir. R. Mensink from Maastricht, " but at NIZO they managed to provide us with food products that met our specifications and still had an acceptable flavour, texture, stability and shelf-life."

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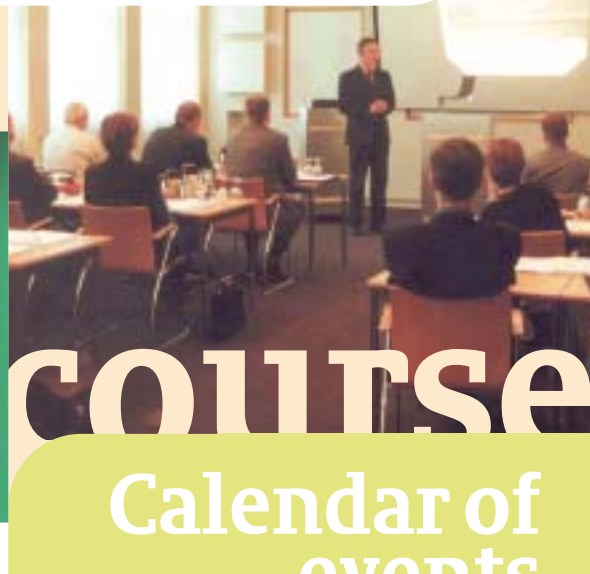

Calendar of events

2002

- **September 18** | Presentation entitled 'Innovative upstream and downstream processing of health ingredients' By Dr. Gerhard de Ruiter during the Health Ingredients (Hi) conference and exhibition. *Paris.*
- **September 20** | Open NIZO Lecture entitled 'Visualising ingredients in action' by Dr. Hans Tromp *at NIZO food research, Ede*
- **Oktober 2** | NIZO-leatherhead training course 'Folate - a vitamin in the spotlight' *at NIZO food research, Ede*
- **November 22** | Open NIZO Lecture entitled 'NIZO Premia: Model-based software to streamline R&D and time to market' by Dr. Peter de Jong *at NIZO food research, Ede*
- **November 7** | NIZO-leatherhead training course 'Rapid detection of yeasts and moulds' *at NIZO food research, Ede*

2003

- **June 11-13** | 3rd NIZO Dairy Conference on 'Dynamics of Texture, Process & Perception' (www.nizodairyconference.com) sponsored by Elsevier, scientific organisation by NIZO food research. *at Papendal national sports centre, Arnhem.*

For more information about any of the above events: contact us at info@nizo.nl

Colophon

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