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Nano food and beverage supplements

How many in the market?

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When considering new publications regarding nanotechnology applied to food supplements, it can be of interest to have an idea of what and how many products are already on the market. To this purpose we have consulted the online inventory of the Project on Emerging Nanotechnologies (PEN, www.nanotech-project.org). While not comprehensive, this inventory gives the public the best available look at the 1000+ manufacturer-identified nanotechnology-based consumer products currently on the market in different fields (Fig. 1).

Products in the inventory are grouped according to the main relevant categories (Fig. 1). The largest category is health and fitness, with a total of 738 products. Within this category, the cosmetics, clothing and personal care sub-categories are now the largest in the inventory.

A search for 'supplements' in the food and beverage category gives 105 entries, with the supplements sub-category comprising 60 products, of which 82% are found in the US market (minerals, vitamins, curcumin, resveratrol, CoQ10, etc.).

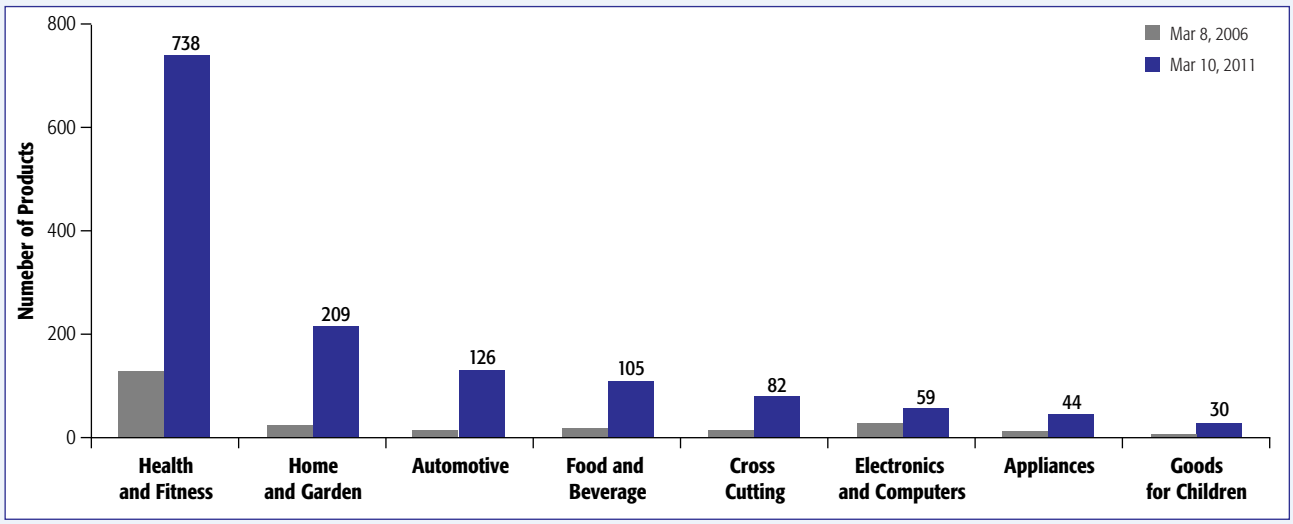

Figure 1 Number of products in the inventory of the Project on Emerging Nanotechnologies (www.nanotechproject.org), according to category

The inventory was updated in March 2011 and now includes 1317 products; it has grown 521% since March 2006. The inventory now includes products from 30 different countries: Europe (the UK, France, Germany, Finland, Switzerland, Italy, Sweden, Denmark, the Netherlands), with 367 products, has overtaken East Asia (including China, Taiwan, Korea, Japan; 261 products) as the second greatest contributor of manufacturer-identified nanotechnology-enabled consumer products, although the USA still contributes the most (587). Other countries (Australia, Canada, Mexico, Israel, New Zealand, Malaysia, Thailand, Singapore, the Philippines, Malaysia) account for 73 products.

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Of the remaining countries:

- Three products are from China (two Nano Oxygen, Sanqing Oral Liquid, which contains curacao, aloe vera gel and oligosaccharide as main raw materials, and supplemented by chitin, chrysanthemum, *Ginkgo biloba*, black fungus, *Ganoderma lucidum*, cordyceps and more than a dozen traditional Chinese medicinal materials to "eliminate free radicals").
- Two from New Zeeland (Colloidal Silver Liquid, to "boost immune system to assist natural healing").
- One from Canada (NanoSlim, containing corosolic acid, an insulin mimetic).
- One from Israel (Nano-Sized Self-assembled Liquid Structures (NSSL) Supplements).
- One entry from Germany (Aquanova Novasol). It is interesting that the Novasol patent by Aquanova, one of the largest producers of liquid nanostructures, is in fact a system carrier that uses a micelle diameter of about 30 nm to encapsulate

active substances. The NovaSOL® Solubilisates are liquid, and at the same time water- and fat-soluble raw materials and ingredients with micelle structure for vitamins, omega-3 fatty acid, coenzyme Q10, isoflavones, flavonoids, carotenoids, phyto extracts, essential oils, preserving agents, food colouring substances and other bioactive substances.

In conclusion, it seems that, although the issue of nanoparticle safety is still a matter of discussion, the number of nanoproducts in the food supplements market is increasing. Now that the labelling "nano" is mandatory, consumer awareness will further increase. Thus, in the future it would be of interest to verify if these products will be readily accepted by consumers.

Further research on safety of nanomaterials

BASF participates in NanoGEM research project

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How a nanoparticle behaves in the body is determined by the properties of the substance it consists of. The size of the particles is of secondary importance. If a biological effect is present, it can often be weakened by a technique known as functionalisation. These are the results of the NanoGEM (Nanostructured Materials: Health, Exposure and Material Properties) project initiated by the Federal Ministry of Education and Research (BMBF) and involving 19 research institutions and companies, which have been working together for three years (1 August 2010 to 31 July 2013). Research topics included the absorption and distribution of nanoparticles in the human body depending on their size, structure and surface properties. The project, on which the BMBF and industry have jointly spent about €6.5 million, was led by *Thomas Kuhlbusch* of the Institute of Energy and Environmental Technology (IUTA) in Duisburg, Germany.

Altogether 16 different materials were examined by the researchers over the last few years, among other things to find out what happens to different nanoparticles when they are inhaled or ingested and how they behave inside the body. Test substances were silicon dioxide (SiO_2) and zirconium dioxide (ZrO_2), which are applied, for example, in paints to increase their scratch resistance, as well as silver particles (Ag) used in printing inks for solar technology. For the first time, not only the pure particles but also the functionalised particles were tested. In the latter, organic molecules are bound to the surface of the particles to improve properties such as processability, solubility or stability of the products.

The result: "The main factors that determine whether there is a toxic effect are the actual material properties, in this case of silicon dioxide, silver or zirconium dioxide", explained *Wendel Wohlleben*, who headed BASF's activities. The company has contributed to the manufacturing and characterisation of the nanomaterials, analysing the life cycle and toxicity, as well as performing a risk assessment. A toxic effect that was the same for all nanomaterials and triggered alone by the small size could not be verified, emphasised Wohlleben. "One important result of the study is that an existing toxic effect can be reduced through functionalising the nanoparticles by adding a functional group of the kind present in the finished product," he added. This is because potential reactions on the particle surface are shielded by the functional groups. Moreover, some particles are eliminated from the body more easily.

These findings will also help researchers in risk assessments of other nanomaterials. "If this result is confirmed in further studies, in future we would no longer have to examine all differently functionalised particles of a material to conduct a safety assessment, but could organise the materials into groups," said Wohlleben. "A reliable risk assessment would then be easier and take less time." This is a great advantage, especially when studying the effect of nanoparticles that are inhaled.

BASF in a nutshell

BASF is the world's leading chemical company: The Chemical Company. Its portfolio ranges from chemicals, plastics, performance products and crop protection products to oil and gas. We combine economic success with environmental protection and social responsibility. Through science and innovation, we enable our customers in nearly every industry to meet the current and future needs of society. Our products and solutions contribute to conserving resources, ensuring nutrition and improving quality of life. We have summed up this contribution in our corporate purpose: We create chemistry for a sustainable future. BASF had sales of €72.1 billion in 2012 and more than 110,000 employees as of the end of the year. BASF shares are traded on the stock exchanges in Frankfurt (BAS), London (BFA) and Zurich (AN).

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Probiotics and prebiotics

New positive assessments by The Cochrane Collaboration

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In this "difficult" period for prebiotics and probiotics in overcoming the European Food Safety Authority (EFSA) health claim assessment, it seems relevant to quote two recent systematic reviews by The Cochrane Collaboration (CC). They introduce some optimism, at least regarding the prevention of eczema in children and diarrhoea caused by antibiotics.

CC is an international network of more than 28,000 dedicated people from over 100 countries whose work is internationally recognised as the benchmark for high-quality information about the effectiveness of health care. They work together to help healthcare practitioners, policy-makers, patients, and their advocates and carers to well-informed decisions about health care, by preparing, updating and promoting the accessibility of Cochrane Reviews (over 5000 so far), published online in the *Cochrane Database of Systematic Reviews*, part of *The Cochrane Library*.

Prebiotics in the prevention of eczema in children

Allergic reactions (asthma, eczema, urticaria, rhinitis, hay fever) are very common in children and some infants may develop sensitivities to infant formula.

Prebiotics added in infant formula may help to prevent eczema in infants, but it is unclear if they can prevent allergies. This is the conclusion of a recent systematic review, published in the Cochrane Library [1].

Prebiotics are present in breast milk and can be added to infant formula. Among these, the most used in children are non-digestible oligosaccharides, such as fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS), which are present in breast milk in a proportion of 1:9.

The review assessed four randomised clinical trials that compared the use of prebiotics supplementation with a standard infant formula for the prevention of allergies, with a total of 1428 children aged between 4 months and 2 years. Only one study reported a reduction in the appearance of eczema in children receiving GOS:FOS supplementation (9:1, 6.8 g/l) and acidic oligosaccharides (1.2 g/l). Meta-analysis of four studies showed that the overall appearance of eczema was significantly lower (p=0.03) in children who received the milk with the addition of prebiotics, while there was no significant effect for the appearance of asthma (assessed only in two studies) or urticaria (one study).

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In infants at high risk of developing allergies based on family history, considered in one study, a significant reduction was reported in the appearance of asthma and eczema with supplementation with 8 g/l of GOS:FOS (9:1).

Sinn and Osborn (University of Sydney) concluded that infant formula containing prebiotics supplements can help prevent eczema in children under two years, but the quality of the studies is low, and it is not clear whether the use of prebiotics should be restricted to infants at high risk of developing allergies or may have an effect in low-risk populations.

Further clinical trials are required before recommending the use of prebiotics for the prevention of allergy in all formula-fed infants.

Probiotics in the prevention of antibiotic-associated diarrhoea

Antibiotics are widely prescribed, however, they can alter the gastrointestinal flora, leading to reduced resistance to pathogens such as *Clostridium difficile*, causing diarrhoea (CDAD) or colitis.

Probiotics, according to CC, can help to re-balance the intestinal flora and reduce the symptoms of diarrhoea in patients treated with antibiotics [2].

The review included 31 randomised trials controlled with placebo, no treatment or alternative prophylaxis, for 4492 participants. In these 23 studies (4213 subjects, adults and children) the incidence of CDAD was 2% in the group who took probiotics and 5.5% in the control group, with a risk reduction of 64%. The results were not significantly different between children and adults, high or low dose, or probiotic species. In absolute terms, prophylaxis with probiotics prevents 35 cases of CDAD per 1000 treated subjects.

Probiotics reduced adverse events (abdominal cramps, nausea, fever, flatulence, taste alterations) by 20% compared with placebo, at least according to an analysis of the studies that have reported adverse events (26 studies, 3964 subjects).

There were no significant differences regarding the incidence of infections by *C. difficile* (13 trials, 961 participants).

The authors conclude that supplementation with probiotics during antibiotic treatment appears to be a safe and effective way to prevent CDAD, even if it does not reduce the number of people infected by the bacterium. It is assumed that probiotics may reduce the extent of the infection rather than inhibit its colonisation.

However, further studies are needed to define the probiotic strains and doses that provide the best results, and to clarify