ObservatoryNANO

BRIEFING No.18

AGRIFOOD

IMPROVING DELIVERY OF ESSENTIAL VITAMINS & MINERALS

The increase in global population is putting pressure on the food sector. Not only have recent natural disasters caused a price hike in food prices, we see country/continent specific shifts and needs. In Europe the increasing problem of obesity, and malnutrition, are of major concern . Here, cultural trends are leading populations into high fat and high sugar diets with less emphasis on fresh fruit and vegetables, wholegrains, and a variety of protein rich and vitamin/mineral rich produce. These are not always readily available, and in some cases key nutrients are difficult to obtain and thus supplements are required. Alongside the need to promote a mixed diet and a healthier lifestyle, there are certain cases where nutrient supplements are required particularly in poorly soluble compounds. Encapsulation provides a promising approach, and R&D expectations point to a real contribution in increasing the bioavailability of nutrients. Moreover, novel processing techniques are indicating that inclusion into processed foods themselves (so called fortified foods) is a means of including these supplements into the diet of the European citizen.

The Challenge

The large-scale food production system of industrialised countries (and those which are in the transition to industrialisation) has provided cheap and widely available food stuffs, which is coupled to the trend of increasing dependency on processed food for growing populations. The reliance on processed foods is a complex combination of culture, trends, technology, and market. Nevertheless today processed foods form a large part of the diet of industrialised societies. It is recognised that many processed food stuffs often have reduced levels of vital nutrients, through the processing procedure itself, or through secondary effects of cultural tastes and fashions towards processed foods high in salt, fat and sugar.

Access to fresh produce is one approach, but availability may be limited for some sections of society. Price is a also major issue, as has been seen in the early days of organic foodstuffs.

The challenge is to find solutions to provide the necessary nutrients for a healthy lifestyle, while providing a sufficient and sustainable food source. Reduction of fats, sugars, cholesterol, and salt is one driver. The provision of essential nutrients (vitamins, minerals, fatty acids) is another. Indeed, an additional related driver relates to the increasing interest in the development of fortified and functional foods (nutraceuticals) that can fight diseases such as obesity, heart disease, and a variety of cancers.

The Technology

Bioavailability – why is it important?

The term bioavailability refers to the fraction of a substance that is actively available within the body; for most oral doses this definition is interpreted as the fraction of the dose that enters the bloodstream[1,2]. Uptake (or intestinal absorption), on the other hand, refers to fraction of the dose that is absorbed through the intestinal walls. Although both definitions are related, the entire dose that is absorbed through the intestine (uptake) may not be bioavailable due to the various processes involved in the absorption of nutrients. To design effective nanoparticle delivery systems for nutrients, nutraceuticals and related active ingredients, it is necessary to understand the biological processes that regulate uptake and bioavailability.

Which nutrients are the most pressing?

There are a number of nutrients that have been flagged as being important for health, to prevent disease and also to reduce the effects of ailments. Nutrients for which nanoencapsulation will provide added value are those which are poorly soluble in water (the medium in which nutrients are passed through the digestive system) include vitamins, anti-oxidants, carotenoids, omega-3 fatty acids, coenzyme Q10, curcumin, green tea polyphenols, and quercetin.

What does a delivery system need to achieve?

A nutrient delivery system must be able to:

- Contain enough bioactive substance and efficiently retain it during storage, processing, and transport;
- Prevent oxidation or other chemical degradation;
- Be easily incorporated into food and drink without causing a change in flavour, texture, or appearance;
- Be produced by materials generally recognized as safe (GRAS) and conform to good manufacturing practices;
- Show an appropriate cost/benefit ratio;
- Depending on the nutrient, preferably show targeted delivery and controlled release (such as in specific areas of the body).

All of these features should be achieved without inducing adverse effects.

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How does nano-encapsulation help?

With regard to nutritional supplements, nanotechnology has been long used to reduce the particle size of various compounds for improving their absorption. Among several approaches that have proved to be very effective in creating nanoparticles, the best way appears to be through encapsulation. Molecules are separated and then enveloped in the active compound. Such compounds are therefore immediately and effectively absorbed in the body. There are a number of platforms available for this purpose, based on natural and synthetic materials. Nanoemulsions fabricated from food-grade ingredients are being increasingly utilized in the food industry to encapsulate, protect, and deliver lipophilic functional components, such as biologically-active lipids (omega-3 fatty acids, conjugated linoleic acid) and oil-soluble flavors, vitamins, preservatives, and nutraceuticals.

For example dibenzoylmethane nanoemulsions (derived from liquorice) have shown the potential to enhance oral bioavailability threefold compared to microemulsions[3]. Critical to this is the control of interfacial properties which control the stability of droplets (either water or oil) within the emulsion[4,5]. Such systems must be robust enough to withstand food processing conditions, and environmental changes during distribution and handling by the consumer. Finally, one of the main obstacles to using nanoemulsions for foodstuffs is the lack of food-grade surfactants[6].

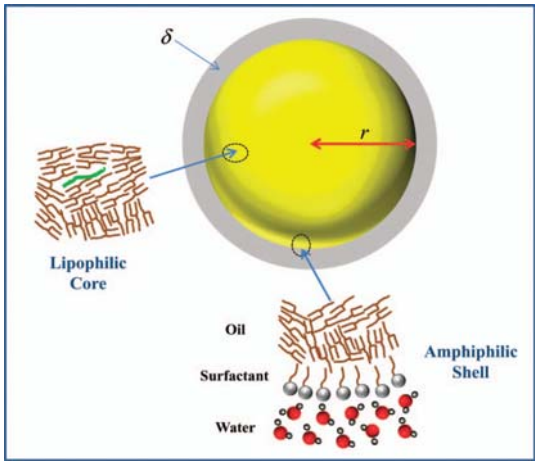

Figure 1: *Schematic representation of the core-shell structure of particles in nanoemulsions[3].*

There are several different compounds, both biogenic and synthetic which are being developed for the purpose of delivering additional nutrients within food. ***Table 1*** summarises the most promising of these.

Impacts

Economic

Growing health awareness, time constraints, and

Material	Description	Potential applications
Nanoemulsions	Made from a variety of lipids or other polymers, droplet size in the order of 100 nm. Relatively stable systems.	Delivery of both hydrophobic and hydrophilic compounds. Possibility of multiple phases and hence simultaneous or sequential delivery of multiple compounds.
Solid Lipid Nanoparticles	Crystalline or semi-crystalline stabilised by a surfactant coating. Made by emulsion technologies. Stable system.	Delivery of hydrophobic materials.
Liposomes	Capsules consisting of lipid bi-layer with aqueous interior. Generally phospholipids, such as phosphatidyl choline.	Delivery of hydrophilic compounds.
Micelles	Droplets of surfactants (lipids or biopolymers) in a liquid.	Delivery of hydrophobic compounds (normally).
Casein	Milk protein that self-assembles into micellar structures.	Delivery of minerals, proteins and vitamins.
Whey proteins	Largely β-lactoglobulin and α-lactalbumin. Can form fibrils, hydrogels, and nanoparticles dependent on processing conditions. Resistant to stomach acid and enzymes.	Delivery of various hydrophilic compounds to the intestinal mucosa. Also can be used to provide nanoscale structure to food (i.e. affect mouth feel).
Chitosan	Carbohydrate isolated from crustaceans. Muco-adhesive, bio-compatible, non-toxic. Forms nanocapsules and hydrogels.	Delivery of different compounds to the oral (e.g. for taste) or to the intestinal mucosa, as part of a multi-component and layered system.
Silica	Bio-compatible and degradable. Can be made highly nanoporous.	Delivery of various hydrophilic nutrients to the stomach.

Table 1: *Some promising nanostructured delivery systems for nutrients.*

the ensuing demand for functional and convenience foods has and will continue to drive growth and development of the food encapsulation market. A recent report[7] estimated that the food encapsulation market is projected to reach about €27.7 billion by the year 2015. Development and application of food-grade nanoemulsions has recently increased because of the demand for an effective systems to encapsulate, protect and release functional food components. Conventional oil-in-water emulsions are currently the most widely used emulsion-based delivery systems in many industrial applications. The small size of droplets (r <100nm) in nanoemulsions means that they do not scatter light strongly and they are able to significantly enhance the bioavailability of encapsulated lipophilic substances. Therefore the best way of applying nanoemulsions as the delivery systems in food, beverage, and pharmaceuticals may be in products where an optical transparency and/or increased bioavailability of an active component is important. Key players in the encapsulation technology marketplace include Advanced BioNutrition Corporation, ABCO Laboratories Inc, Aveka Group, Blue California, Balchem Corporation, Coating Place Inc, Cargill Inc, Encapsys Microencapsulation, amongst others.

Technology Readiness Levels

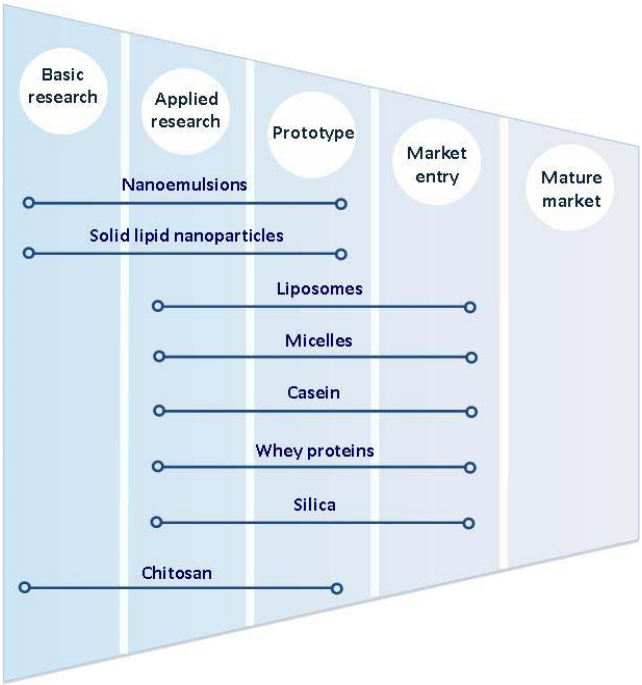

***Figure 2**: TRL levels for nano-enabled encapsulation technologies*

Savings in health care

Venture capital investments are expected to be especially high in the functional foods segment, given the rapidly ageing population and growing demand for foods with disease prevention benefits. Preventative measures against a variety of dietary based diseases and disorders may provide dramatic savings on the cost of healthcare on the state – a growing concern due to the increasing dominance on convenience foods which have low nutritional value and are high in salts, fats and sugars fuelling obesity. In addition, nano-enabled nutraceuticals could provide an alternative approach to certain disease therapies (in cancer, arthritis, diabetes, heart disease).

Impact on the European Citizen

There is a high potential value coming from encapsulation for health via fortified foods, improved nutritional supplements, and nutraceuticals. These promise great improvements to quality of life and general health.

Challenges

Public opinion, ethical concerns & legislation

There is much public debate on nano-ingredients in food, including some on encapsulation. Friends of the Earth (FoE) acknowledge that nano-encapsulation may reduce the quantities of additives required, to the benefit of food processors. On the other hand, the authors are concerned about potential health risks due to a greater potential for cellular uptake of nanomaterials and their greater chemical reactivity. They call for a moratorium on the further commercial release of food products that contain manufactured nanomaterials until nano-specific safety laws are established and the public is involved in decision making. FoE are also concerned that nano-additives might encourage consumption of unhealthy processed food[8].

There has been a controversy between the European Commission, Parliament and Council on the Novel Foods repeal Regulation (EC) No 258/97 which collapsed at the end of March 2011[9] (due to issues unrelated to nanotechnologies). Because of this nano-ingredients in novel foods may not be regulated for many years and are not subject to European labelling requirements for the time being. Food manufacturers are left with no clarity on what is allowed and not allowed in Europe. There is also a difference of opinion on the suitability of current risk assessment procedures for nanoingredients in food. However, agreement has been reached over nanolabelling and a preliminary definition of nanomaterials[10]. In general, the public is more concerned about health and ethical aspects of nano-ingredients in food than in external nanotechnologies.

Common bioethical concerns such as 'naturalness ' and the acceptability of 'playing God' are also relevant to encapsulation of food ingredients where modification is the key element of the technology.

Other issues have also been raised by ethicists, such as the proliferation of nutritionally-engineered foods is deemed to contribute to a trend of nutrification. This means that the value of food is increasingly reduced to its nutritional contents[11].

EHS Impacts and legislation

With regard to the exposure for consumers, the fate of the vectors that carry the encapsulated nutraceuticals is unclear, the short, and longer, term effects needs to be further explored. Knowledge about the toxicity of nano-vectors as well as their overall bioavailability throughout the body is still relatively sparse. During manufacturing of nano-structured delivery systems, workers may potentially be exposed to nanomaterials. On disposal or after excretion out of the human body, exposure of surface water and soil is possible. Hazard and risk assessment of nanomaterials should be completed on a case-by case basis.

EU Competitive Position

There is a large market in Europe for providing low fat/sugar options as part of the drive for greater convenience in food products. Many European companies are becoming involved, including some traditional food production firms. For example, "La Morella Nuts", a firm located in Spain which has a history in confectionary and nut ingredients, has been involved in R&D in nanotechnology in relation to functional foods. Also, the Italian pasta firm "Antonio Amato" has invested time in encapsulation via participation in the FP7 NANOFOODS project. In Israel, there are a number of companies dealing in this area; "Nutralease" develops micelles that can be used to encapsulate a variety of food related substances, such as vitamins, aromas, etc. (www.nutralease.com). "Karmat Coating Industries Limited" has 20 years of microencapsulation experience and has been active in exploring nanoencapsulation possibilities. In Europe, one of the major players is AQUANOVA, based in Germany, it provides nano-micelles for delivery of many types of nutraceuticals.

Finding evidence of nano-enabled nutraceuticals on the market is not easy. A number of products labelled as "nano" are on the market already. "RBC Life" offers a number of nanobased nutraceuticals such as its Nanoceuticals™ range (including Silver 22 and Microhydrin®) or its Nanogreens (www.biopharmasci.com/supersorb) which uses encapsulation with liposomes.

Another product labelled as "nano" are the "Nano-Go Nutraceutical" products (www.canyonworldquest.com/press.html). What is defined as nano, and what is the nano-component here is unclear. However, these kinds of products are illustrative of the vision within certain elements of industry with regards to nano-enabled nutraceuticals.

Summary

- Nanoencapsulation offers tremendous potential in providing a means to deliver difficult-to-attain nutrients in fortified food products.
- Nutraceuticals which provide nutrients that have a clear therapeutic or disease prevention effect promise to be better delivered and more bioavailable through nanoencapsulation
- Consumers appreciate these potential benefits, whereas their concerns mainly occur around food modification in general, and thus is not particular to nanotechnology, alongside this, the emphasis on modification/fortification of foods may distract resources from providing organic, fresh and unprocessed foods.
- Legislation is the biggest barrier to commercialisation here; it is difficult to provide guidelines for regulation and standards.
- The lack of comprehensive knowledge of toxicity of nanomaterials is a broader issue, but becomes specific in the case of encapsulation for food stuffs precisely because the technology aims at increasing bioavailability.
- European research in this area is quite strong, and companies involved in nano and micro-encapsulation are visible. But without a clearer regulatory landscape, growth in this area and the exploitation of research findings in nano-encapsulation will be considerably limited.

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