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Marine nutraceuticals: glucosamine and omega-3 fatty acids

New trends for established ingredients



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ABSTRACT: Glucosamine and long-chain omega-3 lipid are the two most widely consumed marine nutraceuticals. These ingredients have been used as dietary supplement ingredients for many years, but are now becoming important functional food and beverage ingredients. The production of GRAS and vegetarian glucosamine has led to increased use of this ingredient in beverages in particular. For long-chain omega-3 lipid the development of stabilisation technologies has been critical for the increased use of these lipids in functional foods. The development of new sources of both of these ingredients, together with novel delivery and application technologies, will continue to drive increased consumption of these marine nutraceuticals, in particular as functional food and beverage ingredients.

KEYWORDS: Glucosamine, omega-3, EPA and DHA, marine nutraceuticals.

INTRODUCTION

Glucosamine is primarily consumed as a dietary supplement for the prevention or treatment of osteoarthritis, which affects about 21 million Americans and is the most common form of arthritis worldwide. Although the clinical evidence to support the efficacy of glucosamine is not conclusive, it is very strong. The two largest clinical trials on glucosamine for osteoarthritis were published recently. The NIH-sponsored multicenter study, known as the glucosamine/chondroitin arthritis intervention trial (GAIT), compared 1500 mg/day of glucosamine hydrochloride alone, 1200 mg/day of chondroitin sulphate alone, glucosamine hydrochloride and chondroitin sulphate together, the drug Celecoxib (Celebrex), and a placebo for 24 weeks (1). The study found that for a subset of participants with moderate-to-severe pain, glucosamine combined with chondroitin sulphate provided statistically significant pain relief compared with placebo, with about 79 percent of participants having a 20 percent or greater reduction in pain versus about 54 percent for placebo. The second recent study, the glucosamine unum die efficacy (GUIDE) trial, was carried out on 300 participants in three groups, one taking 1500 mg/day of glucosamine sulphate, the second 3000 mg/day of acetaminophen, and the third a placebo for 24 weeks (2). Results indicated that glucosamine sulphate was more effective than either placebo or acetaminophen at reducing pain. A recent systematic review and economic evaluation of the clinical effectiveness of glucosamine and chondroitin supplements concluded that there is evidence that glucosamine sulphate shows some clinical effectiveness in the treatment of osteoarthritis (3). Strong clinical support and consumer awareness has enabled glucosamine to become an established dietary supplement ingredient with about a 10 percent worldwide growth rate from 2003 to 2008. Sales in the USA alone were \$872M in 2008 and about \$2B globally. Glucosamine has had less success as a functional food

ingredient than as a dietary supplement ingredient, partly because the major source of glucosamine is from shrimp shells and is not Generally Recognised as Safe (GRAS) in the USA. Recent new sources of glucosamine with GRAS status, together with improved food and beverage formulation, have increased the use of glucosamine in food and beverages. A summary of new glucosamine sources and food and beverage formulations will be given below.

The health benefits of the long-chain (LC) omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are established and have been the subject of numerous reviews (4-7). Although the clinical evidence is strongest for cardiovascular benefit LC omega-3s have a variety of health benefits and are

considered wellness products, leading to relatively good success in functional foods. Approximately 300 new LC omega-3 fortified food products were introduced worldwide in 2006, 400 in 2007 and 700 in 2008, with global retail sales of these fortified foods expected to grow from about \$5B in 2008 to \$8B in 2012 (8). Major brands such as Minute Maid, from Coca Cola, and Tropicana, from Pepsi, have launched LC omega-3 fortified products. In addition to the functional food market, adding DHA to infant formulae has become the industry standard, with DHA fortified formulas representing about 70 percent of the total \$9B global infant formula market. The dietary supplement market for LC omega-3 also remains strong, with the majority of ingredient in this segment being derived from fish. The major source of DHA in infant formula is supplied by single cell organisms (SCO), mainly from the organism *Cryptocodinium cohnii* produced by Martek Biosciences. LC omega-3 fortified food normally requires stabilisation through the use of microencapsulation and both SCO and fish sources are being used in foods. New sources of LC omega-3 fatty acids, together with improved microencapsulation and delivery technologies, are helping to expand the use of this ingredient in foods. A summary of new sources and delivery technologies will be given below.

PRODUCTION OF GRAS GLUCOSAMINE

Recently vegetarian sources of glucosamine have been developed, leading to the launch of Cargill's Regenasure® glucosamine derived from the fungus *Aspergillus niger*, Cyanotech's JointAstin® produced through fermentation, and products from DNP International and China-based Hygieia Health. In 2007 Cargill obtained GRAS status for Regenasure® making this product allowable for use in mainstream food and beverage applications. In addition to being GRAS Regenasure® is vegetarian and kosher, overcoming key industry hurdles for use in foods in the USA.

Glucosamine is derived from chitin, the second most abundant polymer on earth after cellulose. Chitin is primarily derived from shrimp and crab shells. However, chitin is also abundant in the cell walls of fungi such as *Aspergillus sp.*, *Penicillium sp.* and *Mucor sp.* Regenasure® is derived from the common *Aspergillus sp.*, *Aspergillus niger* (9). Glucosamine is produced from fungal biomass in a similar manner to how it is produced from shrimp shells. That is, the biomass is deproteinated using aqueous sodium hydroxide. Washed material is subsequently depolymerised using hydrochloric acid, and the glucosamine precipitated, washed and dried. Enzymes such as chitinases can be used for the depolymerisation step, but this method results in a more expensive process and so is not used industrially (10).

GLUCOSAMINE FORMULATION IN FOODS

Beverages containing glucosamine have been on the market in the USA for several years. One of the earliest glucosamine beverage products was Joint Juice®, which contains 1500 mg of Glucosamine hydrochloride per serving. Because of the non-GRAS status of shrimp shell derived glucosamine, products such as Joint Juice® were starting to be targeted for review by the FDA. However, the introduction of Cargill's GRAS ingredient enabled beverage makers to replace their non-GRAS ingredient and overcome a key regulatory hurdle to having their products accepted in the mass market. The GRAS status of Regenasure® has also enabled large multi-national companies with strong brands such as Coca-Cola to add glucosamine to their beverages. In 2007 Coca-Cola North America launched Minute Maid Active, which contains 750 mg of Glucosamine hydrochloride (Regenasure®) per serving as part

of the Minute Maid Enhance Juice line. In 2000 Pepsi purchased SoBe which sold functional beverages, including a glucosamine containing beverage for joint health. However, Pepsi has not yet launched a glucosamine product under its major brands such as Gatorade or Tropicana.

Glucosamine is readily formulated into beverages since it is a highly water soluble, colourless ingredient, with little taste. Numerous beverages containing glucosamine

There is still considerable room for market expansion of LC omega-3 fortified foods and the next few years will determine how successful this ingredient will be in foods

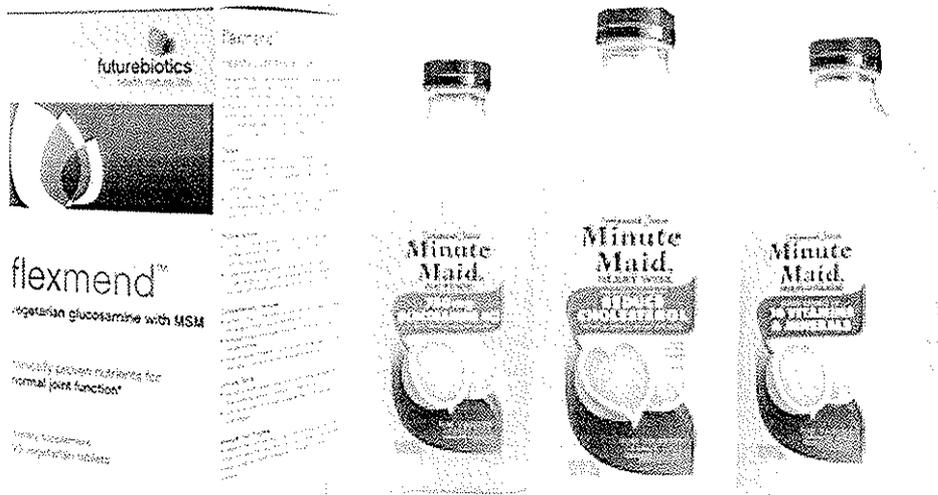
have been launched in the last few years, some of which are shown in Figure 1. Glucosamine has also been formulated into several food products, including cereal and yogurt. However, glucosamine beverages have been much more successful than glucosamine foods. The total dollar volume of glucosamine containing foods and beverages is unclear. However, it is clear that by far the major component of the \$2B glucosamine market is dietary supplements and functional foods and beverages sales are still small. Although there is high consumer awareness of glucosamine, it is not considered a general wellness ingredient, which could inhibit its growth in mass market food and beverage applications. It will be interesting to watch the growth of this category over the next several years, especially with some suppliers getting European approval for their vegetarian glucosamine ingredients, including China-based Hygieia Health with GlucosaGreen®, although not yet

for food use. Foods and beverages are targeted at a healthy population and can be consumed by a variety of people at various dosages. Cargill has applied for novel food ingredient status in Europe for Regenasure®, but this was delayed by the UK's Food Standards Agency due to a lack of information on whether it would affect people with diabetes. In late 2009 the European Food Safety Authority has denied further health claims for glucosamine since claims need to show a reduction of disease risk and there is lack of clinical data on the ability of glucosamine to prevent cartilage degeneration outside of patients with osteoarthritis. Such regulatory decisions will make it difficult for glucosamine food and beverages to launch successfully in the EU.

NEW SOURCES OF LONG-CHAIN OMEGA-3 FATTY ACIDS

LC omega-3 fatty acids from fish oil are widely used in functional foods. New alternative sources of LC omega-3 will lead to expansion of the use of these fatty acids. These sources are primarily novel SCOs and genetically-modified plants. For example, Du Pont has developed both EPA and DHA producing yeast strains through metabolically engineering *Yarrowia lipolytica*. Desaturase and elongase genes were introduced into the oleaginous yeast to synthesize these fatty acids under fermentation conditions.

Figure 1. Examples of glucosamine products containing Regenasure®.



These genetically modified yeasts can produce up to 55 percent LC omega-3 in the accumulated oil under optimized conditions (11). Numerous other groups are targeting the development of natural and genetically modified SCO for the production of LC omega-3 fatty acids. A number of groups are also targeting the development of plant sources. The most advanced is Monsanto, who have developed a genetically modified soybean oil rich in omega-3, and have recently had a positive response from the FDA with regard to their GRAS notice no. GRN 000283, essentially ruling that this modified oil is safe to eat. However, the Monsanto soybean product contains stearidonic acid rather than EPA or DHA, and so relies on the conversion in the body to especially EPA. Conversion from stearidonic acid to EPA is more efficient than from α -linolenic acid, the most common plant omega-3, but is still very inefficiently converted to DHA.

Other companies, such as the world's largest chemical company BASF, are attempting to genetically modify plants to produce EPA and DHA. BASF is taking genes from marine algae and inserting them into canola and flax with the aim of producing canola or flax oils containing EPA and DHA. DuPont is working on producing genetically modified soya beans that are capable of converting ALA into EPA and DHA, using genes from the fungus *Saprolegnia diclina*, and have achieved up to 40 percent weight of the oil as LC omega-3 (12). The two key issues for commercialisation of these sources of LC omega-3 are consumer acceptance of genetically modified oils and price competitiveness with relatively low cost fish oils.

NEW MICROENCAPSULATION STRATEGIES FOR DELIVERY OF LC OMEGA-3 TO FOODS AND BEVERAGES

For many food applications microencapsulation is a necessary strategy for stabilising the sensory properties of LC omega-3 lipids, whether these lipids are derived from fish, microbial or genetically modified plant sources. Oils rich in EPA and DHA rapidly oxidise to form aldehydes with unpleasant taste and odour, which can make food unpalatable. For example, the LC omega-3 oxidative degradation product c-4-heptanal has a burnt fishy flavour at levels as low as 0.04 ppm, while t,c-3,6-nonadienal has a fish-like flavour and t,c-2,6-nonadienal has a green, fresh fish-like flavour at levels as low as 0.01 ppm. The most common method of stabilization these oils is through the use of microencapsulation to protect the oil from exposure to light and oxygen, effectively inhibiting the initiation of free-radical based oxidation of EPA and DHA. Several microencapsulation technologies are available and have been applied to fish oil to varying degrees of success. These include spray-dried emulsions, gravity-flow dry blending, fluidized bed coating, molecular inclusion, liposome entrapment and single- and multi-core complex coacervation (13). The most commercially developed processes are spray-dried emulsions and complex coacervation. Producing a spray-dried emulsion involves making an oil-in-water emulsion in the presence of protein or carbohydrate and spray drying the emulsion. Some limitations of spray-dried emulsions are that the particle size is normally large, the oil payload is low at around 30 percent, and the level of surface oil can be high. Clover Corporation of Australia has successfully applied a spray dried emulsion

ingredient, which is stabilised using Maillard chemistry to cross-link protein and carbohydrate, to a variety of food products. This technology was developed by Food Science Australia and CSIRO (14). Martek has taken advantage of the versatility of shell material capable of forming spray dried emulsions to offer both protein and carbohydrate based encapsulated DHA, thereby satisfying Kosher, Halal, vegetarian and non-allergenic requirements.

A novel variation of complex coacervation was developed by Ocean Nutrition Canada using a controlled aggregation process to form an agglomeration, followed by the controlled formation of an outer shell surrounding the agglomeration, to produce a multi-shell particle (15, 16). This method of "multicore" complex coacervation results in a high oil content of 60-70 percent by powder weight, leading to lower cost and less powder per serving to obtain a specific dosage. Multicore complex coacervation also leads to very low surface oil, probably because a shell is formed around the coacervate after agglomeration has occurred, improving sensory performance. However, a disadvantage of complex coacervation is that the shell material is currently limited to gelatin. Both a positively charged polymer and a negatively charged polymer are required for complex coacervation and certain gelation and gel setting properties are necessary for successful shell formation. Recent work at Ocean Nutrition Canada has led to the development of a whey protein based complex coacervate product, although this is still in development (17). Figure 2 compares the physical structure of the whey protein and gelatin powders.

The development of new sources of both of these ingredients, together with novel delivery and application technologies, will continue to drive increased consumption of these marine nutraceuticals, in particular as functional food and beverage ingredients

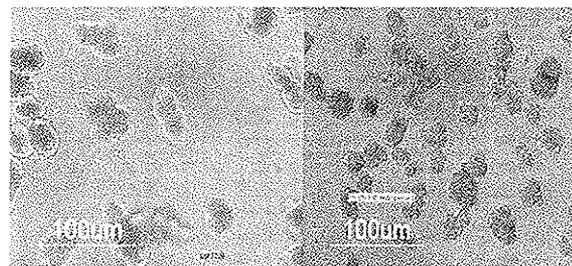


Figure 2. Comparison of Gelatine (left) and Whey protein (right) LC omega-3 powder produced using complex coacervation (thanks to Ocean Nutrition Canada for images).

CONCLUSION

Glucosamine and LC omega-3 lipids are by far the most widely used marine-derived nutraceuticals. Glucosamine is an established supplement ingredient but is only just starting to be used in food products. Glucosamine is having some success in beverage applications, particularly in the USA where GRAS status has been obtained for a vegetarian version. Further expansion of glucosamine as a functional food ingredient will depend upon an ability to get novel food status in a variety of countries. Also, glucosamine is not a general wellness ingredient, but rather a product targeted at osteoarthritis. This will inhibit its growth in foods, partly due to an inability to get health claims due to a lack of data outside of patients with osteoarthritis, and partly due to the difficulty in marketing a disease specific ingredient into foods. Glucosamine will likely have some success in targeted areas such as sports beverages, but the jury is out as to whether this ingredient can effectively penetrate into mass market food

and beverages despite the development of vegetarian sources and the ease of formulating with glucosamine. Omega-3 fatty acids have had more success than glucosamine in foods, partly due to consumer perception of these ingredients as general wellness products. Alternative sources other than fish oil are moving into the market, but the two major hurdles are the generally high price of these sources and their being derived from genetically modified sources. In terms of delivery technologies, these are improving all the time, and the range of foods available that are fortified with omega-3 oils rich in EPA and DHA is increasing partly due to improved stabilisation technologies. There is still considerable room for market expansion of LC omega-3 fortified foods and the next few years will determine how successful this ingredient will be in foods.

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