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Nanotechnology-Enabled Dietary Supplements

By Dónal P. O'Mathúna

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NANOTECHNOLOGY IS A BROAD FIELD OF RESEARCH AND DEVELOPMENT that is defined by its focus on the nanometer (nm) scale. This is generally agreed as covering items in the 1-100 nm range.[1] Nanotechnology is receiving significant funding from governments, private corporations, and investors around the world. Billions are being invested in nanomedicine with the expectation that many new medical and pharmaceutical products will be developed. This investment is already leading to nano-enabled medical products that have annual sales of billions of dollars.[2]

This general growth of interest in nanotechnology has been noticed by some within the dietary supplement industry. A growing number of what are called nanoceuticals, or nanotechnology-enabled dietary supplements, have already entered the market.[3] Given that these are regulated as dietary supplements and not novel drugs, concerns have been raised about their potential risks and uncertainty about side effects. As more of these nanoceuticals become available to patients, clinicians will need to understand the complexities they introduce and how best to advise patients regarding their usage.

Nanotechnology

Nanotechnology includes a wide range of technologies and substances. Objects with dimensions in the nanoscale range include strands of DNA (about 2 nm wide), proteins (many are 5-50 nm wide), viruses (about 75-100 nm), and a range of new nanomaterials called quantum dots (10-100 nm), carbon nanotubes (1.4 nm wide), buckyballs (0.7 nm in diameter), and various other nanoparticles.[1] Most bacteria and human cells are larger than nanoscale, while most individual atoms are smaller than nanoscale. For example, gold atoms are about 0.3 nm wide. However, gold nanoparticles can be made with various diameters that fall within the nanoscale.

Part of what has generated interest and excitement about nanoparticles is their unique properties. The chemical, physical, and biological properties of a substance often differ depending on whether their particles are nanoscale or larger, "bulk" scale. Particles smaller than nanoscale are dominated by quantum effects, whereas particles larger than nanoscale are dominated by their bulk properties. Within the nanoscale range, particles have a combination of quantum and bulk properties, which converge to give nanoparticles unique and interesting attributes.

One distinctive feature crucial for nanomedicine is how nanoparticles interact with cells and living tissues. Molecules that are smaller than nanoscale (like many drugs) enter cells by passive diffusion. Their biological properties are strongly dependent on their solubility and concentration in tissues and fluids. Nanoparticles, however, interact with cells in ways that resemble similarly sized biomolecules like proteins.[4] This opens up opportunities to develop nanoparticles that can access areas of the body that drugs previously had difficulty reaching, such as crossing the blood-brain barrier. Once in the circulation, a "rule of thumb" suggests that nanoparticles < 100 nm in diameter can enter cells, those with diameters < 40 nm can enter the cell nucleus, and those that are < 35 nm can pass through the blood-brain barrier and enter the brain."[5]

This permeability also raises concerns that nanoparticles may accumulate in tissues or organelles where they may cause toxic effects. Using the example of gold again, bulk gold particles are chemically inert and safe in the body. However, gold nanoparticles are taken up by cells and accumulate in their nuclei, with 50 nm gold nanospheres being absorbed by cells more rapidly than smaller or larger nanoparticles in the 10-100 nm range.[6] How these may affect cells is still under investigation. However, "the very same properties that make nanoparticles potentially useful for industrial and biomedical applications have also become a safety concern."[7] Given the surrounding excitement and uncertainty, how best to proceed with nanomedicine is raising challenging ethical issues, not the least of which when applied to dietary supplements.

Nanotechnology Applications

Nanotechnology promises to impact most areas of science and technology, including medicine and pharmaceuticals. Nanotechnology has made a significant contribution to developments with personal electronic devices. The small, faster, higher capacity computers, mp3 players, and cell phones owe much to nanotechnology. New production methods allow the manufacture of antibacterial coatings, self-cleaning windows, and stronger, lighter materials.[1]

In many ways, the field is highly technical and in its early stages of development. While it promises to yield many interesting devices and products, most of these are years away. However, some applications of nanotechnology are already available to consumers. Marketers in various areas have seen "nano" as a prefix that makes a product attractive.

Far Out Nanoceuticals

While many applications of nanotechnology are legitimate, some are claiming that nano-enabled products will be the answer to all our problems: a literal fountain of youth.[8] A growing number of nanoceuticals is already on the market. One consumer advocacy group reported that between 2006 and 2009 the number of nanotechnology-based dietary supplements on the U.S. market went from 11 to 44.[9] One product uses Microcluster® Technology to make silica spheres as small as 5 nm.[8] In the presence of water and nutritional supplements, the nutrients are enclosed within the nanospheres. According to the manufacturer, when the liquid is consumed, the nanospheres enter the cells of the body, release their nutrients and pick up waste compounds, thus bringing health and vitality. However, the only evidence provided to support the claims is anecdotal.

Another product claims to combine the benefits of a Thai herb, *Pueraria mirifica*, with nanotechnology.[10] The extract of the herb is enclosed within nanosomes, which are said to be more efficiently absorbed by the skin. The "Nano Breast Serum" is purported to provide instant breast enhancement and improve firmness.

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A facial cream that contains "about 1 billion nano gold powder grains" is marketed as an anti-aging cream that moisturizes the skin and prevents wrinkles.[11] Such is the flavor of the claims made for these nanoceuticals.

During the earliest phase of development of any new technology, the claims are grand, but the substance can be slim. Such a scenario can leave patients vulnerable to hype or harm. Maybe they are receiving an early application of a new technology with great potential. But they might also be buying into marketing schemes that seek undeserved acclaim by riding the coattails of legitimate nanotechnology advances. At the same time, people can thereby be deceived by hype, misled by unfounded claims, or exposed to unwarranted risks.

Pursuing Clinical Studies

Even while some products make extravagant claims, other developers and researchers are moving down the slow, careful path of conducting clinical research on nanotechnology-enabled dietary supplements. Coenzyme Q10 is available as a dietary supplement with evidence of therapeutic potential. Newer formulations have overcome earlier bioavailability problems. In addition, nanoparticles of coenzyme Q10 have been made and found to be much more readily absorbed in animal models.[12] Such approaches have been developed for use with conventional pharmaceuticals.[1] In a similar way, a number of Chinese herbs were prepared as nanoparticles and found to have increased solubility, better bioavailability, and targeted delivery, allowing the use of lower doses and longer-acting formulations.[13] Most research to date has been conducted on making the nanoparticles, with little clinical research due to uncertainty about adverse effects. A number of different nutrients have been prepared as nanoparticles to examine their absorption and bioavailability compared to bulk nutrients.[14]

New products that combine dietary supplements and nanoparticles have also been developed. For example, epidemiological research supports an association between drinking tea and cancer prevention, which has led to the identification of several antioxidants with in vitro anticarcinogenic compounds. Likewise, gold nanoparticles are being examined for potential anticancer effects. One group of researchers made gold nanoparticles in the presence of a tea extract.[15] The resulting nanoparticles were coated with tea phytochemicals and did not have the usual clumping problems found with other gold nanoparticles. They had significant in vitro activity against prostate and breast cancer cells, yet were non-toxic in assays for normal cells. Toxicity is a significant problem with other gold nanoparticles because the usual methods of manufacture and stabilization involve harsh chemicals and heavy metals that are extremely difficult to remove and toxic in trace amounts. These problems appear to have been resolved by using tea's phytochemicals in what is being called "green nanotechnology."

Adverse Effects

Underlying the use of nanotechnology with dietary supplements is the ongoing concern about their regulation. One report highlighted that current regulations allow dietary supplements that include nanoparticles to enter the market without prior evaluation of safety or effectiveness.[9] Numerous concerns have been raised about various nanoparticles, with the main problem being a lack of information.[6] Very little is known about the toxicity of most nanoparticles. Human and environmental exposure may be somewhat limited when they occur in coatings or tennis rackets. However, much further precautionary measures are needed when people ingest nanoparticles or rub them on their skin. Such testing is only starting to occur in general, and typically has not occurred with the nanoceuticals already on the market.

Conclusion

Nanotechnology promises to make available a range of improved drugs and supplements. These products will parlay the improved solubility, bioavailability, and targeting that nanoparticles provide to various other compounds. In addition, the production of drugs, vitamins, and supplements as nanoparticles may lead to improved properties. However, the lack of regulation of dietary supplements containing nanoparticles raises serious concerns at the moment. It is possible that some dietary supplements with "nano" on their label may not contain nanoparticles at all. However, when they do, there is little information available currently on their safety (or effectiveness). What information is available points to serious concerns about the potential for nanoparticles to cause adverse effects when ingested.[1] Information on topical application is less clear-cut, with some studies on certain nanoparticles in sunscreens finding no evidence of adverse effects.[16] Until much more toxicological data are available, patients should be advised to avoid oral consumption of dietary supplements containing nanoparticles. ■

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Fast Food Fallacy: Diet and Cost

ABSTRACT & COMMENTARY

By Russell H. Greenfield, MD, Editor

Synopsis: *Using a unique model based on a single parent raising one child, researchers showed that following a carefully chosen whole foods diet is less expensive than a convenience/fast food diet. Unfortunately, for people without means, even a healthy diet cannot be sustainably pursued without financial support.*

Source: McDermott AJ, Stephens MB. Cost of eating: Whole foods versus convenience foods in a low-income model. *Fam Med* 2010;42:280-284.

THE AUTHORS OF THIS TRIAL SOUGHT TO DETERMINE WHETHER a whole food (healthy) diet was economically feasible when compared to a fast-food (convenience) diet in the absence of federal or state assistance. They created a model based on a single parent raising one child in an urban environment, with Baltimore City chosen as the area representative of at-risk urban populations (median annual income derived from the 2004 census, $29,792). Mean living expenses included rent and utilities, transportation costs, clothing, school supplies, taxes, and anticipated food consumption. Additional food items, entertainment, costs, credit card debt, and health care costs not covered by employers were not included in the analysis. Estimates for child food costs were taken from the U.S. Department of Agriculture (USDA) Cost Calculator. Costs were calculated for age 1-17 for a single parent household with income less than $58,670, the lowest available income option.

Daily food intake was derived from recommendations from the American Heart Association and the American Academy of Pediatrics, and costs associated with a whole foods diet were presented as retail averages from three large supermarket chains in Baltimore, with the least expensive options used in each food group (generic, frozen, bulk, and canned products). Convenience diet costs were taken directly from a large, multinational fast-food chain. Breakfast meals included a sandwich, hash-brown potatoes, and coffee or juice. Lunch and dinner meals included a sandwich, medium-sized fries, and a 21-ounce carbonated beverage. A representative children's meal included a sandwich or chicken-based bite-sized nuggets, small French fries, and a small carbonated beverage.

The number of calories per ounce of food and cost per calorie were computed for the average healthy diet. Caloric values for fast food items were obtained using on-line nutritional information and cost per calorie computed. Only adult diets were considered in this part of the analysis.

Annual food costs associated with the healthy diet model were $5,019. Average child food costs were estimated to be about $191 per month, or approximately $2,290 annually. Based on an average daily intake of 1,800 calories as recommended by the USDA, annual estimated food costs for an 18- to 35-year-old adult was $2,730 (about $227 per month). Notably, dairy products comprised the largest percentage (> 35%) of adult food