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NEWSLETTER
September 2006

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FOOD NANOTECHNOLOGY

G.A. Burdock, Ph.D. and B.A. Magnuson, Ph.D.

The word "nanotechnology" has evolved beyond a buzzword for marketers and entrepreneurs. Nanotechnology (often abbreviated "nanotech") in some form is currently represented in yearly sales of over $32 billion in products. At present, only a few familiar consumer end products, such as sunscreens, use nanotechnology. Although promising, there are presently only a few applications of nanotechnology in the areas of medicine, food, and agriculture. This lack of applications will not remain as such much longer; the Helmut Kaiser Consultancy estimates that the yearly worldwide nanotech food market may total over $20 billion by the year 2010. This trajectory for increased human exposure provides us with a narrow temporal window to develop a better understanding of nanotechnology and develop some basic safety principles. This is a lull that we must put to good use, because the application of nanotechnology and development of nano-sized particles is not capital intensive (*i.e.,* almost anyone can get started). Additionally, the application of nanotechnology to foods could be initiated by those more interested in a spike in sales than in the long-term effects on the public or the technology itself. Burdock Group is currently investing the time to develop expertise in the toxicology of nanoparticles. Often, the most difficult concept to grasp about nanotechnology is the size scale. A favorite comparison is "a nanometer is to a meter, as the diameter of a dime is to the diameter of the earth." But at this size, some of the basic rules get changed. At the nanoscale, the physical, chemical, and biological properties of materials differ in fundamental ways from the properties of the bulk matter from which the nanosized particles (NSPs) are derived. For example, nano-particulated gold is no longer yellow, but blue in color; it is no longer chemically inert, but may act as a catalyst; and it melts at 200°C instead of 1200°C. Truly, it is as if another "dimension" were discovered for the properties and application of conventional substances. NSPs added to plastics or steel can make the product tens of times stronger. Electrical conductivity of substances can be

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THE ARTICLES FEATURED IN THIS ISSUE ARE SUMMARIES OF PRESENTATIONS GIVEN BY BURDOCK GROUP MEMBERS AT THE 2006 IFT SYMPOSIA

Burdock Group Attending SupplySide West International Trade Show and Conference in October.
See page 2 for details….

INSIDE THIS ISSUE

WOMEN'S HEALTH AND FUNCTIONAL FOODS

by
Ioana Carabin, M.D.
Women's Health Sciences Institute, Inc.

The concept of *functional foods* dates back to the time of Hippocrates, the father of medicine, who said, "*Let food be thy medicine and medicine be thy food.*"

In 1994, the Institute of Medicine (IOM) defined functional foods as *any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains*. To date, the Food and Drug Administration (FDA) does not have a definition for functional foods. After all, functional food is food, and as such the same laws covering the safety of conventional foods govern functional foods.

However, when talking about functional foods, most of us think primarily of their claimed efficacy (e.g. a health claim). A *health claim* has two essential components: a *substance* (food, or food component, or dietary ingredient) and a *disease* or *health related condition*. Therefore, claimed efficacy can be made for dietary ingredients or food ingredients used in dietary supplements or functional foods. As with dietary supplements, claims about the health benefits of functional foods must be based on scientific data. Claims can also be made for specific segments of the population, in which case the scientific data necessary for claim substantiation needs to be appropriate. Consequently, claims made for functional foods can target women, which according to the Census Bureau 2000 report account for just over one-half of the U.S. population. Women are identified as one of the most important consumer groups for functional foods, because they have more specific health and nutrition needs than men, such as during pregnancy, lactation, menstruation and menopause. Therefore, it is generally recognized that

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IN THE NEWS...

Burdock Group Heads West

Burdock Group will be attending the SupplySide West International Tradeshow and Conference, which will be held at The Venetian & Sands Expo in Las Vegas, Nevada from October 18th–20th. Stop by our booth (#4076) to learn more about how we can provide regulatory and scientific solutions for your products.

To set up a 15-minute complimentary consultation with one of our experts, contact Ms. Shirley Reul, Client Relations Coordinator, at sreul@burdockgroup.com.

New Member Joins Burdock Group

Ye Su (Susan) comes to Burdock Group with a Master's degree from the Food Science program at the University of Maryland where she conducted research in functional food development and cancer prevention with food compounds.

She also has a Master's degree in Food Science and Food Processing from the Southwest Agricultural University in Chongqing, China. She brings hands on, practical, and scientific experience and will serve as another valuable resource to the collaboration of scientists at Burdock Group.

Senior Toxicologist Talks About Safety Assessment of Dietary Supplements: Challenges and Opportunities

On June 8th, Dr. Magnuson, Burdock Group's Senior Toxicologist presented at an US FDA/CFSAN meeting. During her presentation, Dr. Magnuson discussed the challenges that dietary supplement manufacturer's face in conducting safety assessments, such as dealing with complex mixtures rather than pure compounds as found in drugs, and problems in standardizing compositions due to variations in natural ingredients. She mentioned that there is also little financial incentive for dietary supplement companies to invest in extensive safety testing, as DSHEA does not require demonstration of safety.

Dr. Magnuson's presentation was well-attended and generated much discussion. Experts at the FDA offered suggestions for how dietary supplement manufacturers can improve New Dietary Ingredient Notifications to reduce the rejection rates. Overall the presentation resulted in an excellent exchange of information and ideas.

Select Pending and Recent Publications

G. A. Burdock, I. G. Carabin and J. C. Griffiths (2006). **The Importance of GRAS to the functional Food and Nutraceutical Industries**. *Toxicology* 221, 17-27.

M.G. Soni, G.A. Burdock, M.S. Christian, C.M. Bitler and R. Crea (2006). **Safety assessment of aqueous olive pulp extract as an antioxidant or antimicrobial agent in foods.** *Food and Chemical Toxicology* 44, 903-915.

J.C. Griffiths and S. Teske (August 2006). **Aiming for the Mainstream.** *The World of Food Ingredients.*

R.A. Isbrucker and G.A. Burdock (IN PRESS). **Risk and safety assessment on the consumption of Licorice root (Glycyrrhiza sp.), its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin.** *Regulatory Toxicology and Pharmacology.*

L.D. Williams, A.E. Glenn, C.W. Bacon, M.A. Smith and R.T. Riley (2006). **Fumonisin Production and Bioavailability to Maize Seedlings Grown from Seeds Inoculated with Fusarium verticillioides and Grown Natural Soils,** *Journal of Agricultural and Food Chemistry* 54, 5694-5700.

B.A. Magnuson (June 2006). **Biting Into Better Health.** *Asia Food Journal.*

See additional publications listed on the back page....or visit www.burdockgroup.com/publications.html

4 out of top 25

Burdock Group published 4 out of the 25 top most recent scientific publications for Food and Chemical Toxicology (listed below).
Source: http://top25.sciencedirect.com

Safety assessment of esters of p-hydroxbenzoic acid (parabens)
Food and Chemical Toxicology, Volume 43, Issue 7, 1 July 2005, Pages 985-1015
Soni, M.G.; Carabin, I.G.; Burdock, G.A.

Safety studies on epigallocatechin gallate (EGCG) preparations. Part 1: Genotoxicity
Food and Chemical Toxicology, Volume 44, Issue 5, 1 May 2006, Pages 626-635
Isbrucker, R.A.; Bausch, J.; Edwards, J.A.; Wolz, E.

Safety studies on epigallocatechin gallate (EGCG) preparations. Part 2: Dermal, acute and short-term toxicity studies
Food and Chemical Toxicology, Volume 44, Issue 5, 1 May 2006, Pages 636-650
Isbrucker, R.A.; Edwards, J.A.; Wolz, E.; Davidovich, A.; Bausch, J.

Safety studies on epigallocatechin gallate (EGCG) preparations. Part 3: Teratogenicity and reproductive toxicity studies in rats
Food and Chemical Toxicology, Volume 44, Issue 5, 1 May 2006, Pages 651-661
Isbrucker, R.A.; Edwards, J.A.; Wolz, E.; Davidovich, A.; Bausch, J.

For a more in-depth listing of our publications, visit www.burdockgroup.com/publications.html

HOT TOPICS

√ **September 18, 2006—*Council for Responsible* Nutrition's (CRN) Annual Symposium on Dietary Supplements:** Dr. George Burdock will be conducting a presentation on the latest regulatory developments surrounding New Dietary Ingredient Notifications at CRN's Annual Symposium in Boston, Massachusetts.

√ **October 12th-13th—Nano4Food Conference**: Burdock Group Sponsor and Participant at the 2nd annual Nano4Food Conference held at the GTRI Conference Center in Atlanta, Georgia. For more info visit www.nanofood.info or contact info@burdockgroup.com.

BURDOCK GROUP WOULD LIKE TO THANK ALL OF THOSE WHO VISITED US AT IFT!

(Continued from page 1—Women 's Health article)

maintaining optimal health varies greatly between genders.

In the United States, health conscious "baby boomers" have shown great interest in functional foods and their claimed benefits, as demonstrated by more than half of the U.S. consumers. The reason is that this generation wants to control their own health and well being, as well as to have more control over their medical treatment and mitigating the increasing cost of prescription medications.

Until recently, the medical community addressed women's health by mainly focusing on the reproductive system. The assumption used to be that men and women reacted comparably to medical conditions and, therefore, drug treatment. However, with the emergence of gender-specific medicine over the last decade, that thought process is shifting. Clinical experience and research show that the diagnosis and treatment of certain medical conditions are different between genders. This realization comes after many women have been misdiagnosed and under treated because they did not present to their doctors with the "classical, textbook" symptoms—symptoms that after all were recorded from observations in men. Below are some interesting findings.

- Women frequently don't have chest pain during a heart attack and complain of more vague, flu-like symptoms. (Women are 11 times more likely to die from a heart attack than from breast cancer).
- Aspirin does not protect women against heart attacks in the same way it does men.
- Women who don't smoke appear to be more susceptible to lung cancer than non-smoking men. Women also tend to get lung cancer at younger ages than men.
- Women metabolize nicotine faster than men do—especially women who are taking oral contraceptives.
- Women are less likely than men to get oral cancer.
- Women are twice as likely to develop gall bladder problems.
- Women are more prone to autoimmune diseases, including lupus, rheumatoid arthritis, and multiple sclerosis.

Research is being conducted in the fields of digestive disorders, general medicine, autoimmune diseases, bariatrics, and heart disease—which are all recognized as either presenting differently or more frequently, or having different outcomes in women than in men. Malignancies are another concern for women of all ages. Cancers unique to women are ovarian, uterine, and cervical. Although breast cancers are predominantly seen in women, the disease can also afflict a very small percentage of men. Cancer is intimately linked to non-genetic factors. Diet, lifestyle, and the environment contribute to approximately three-quarters of all cancer cases.

Interestingly, some conditions, like premenstrual syndrome, pregnancy, lactation, and menopause, are purely stages in a woman's life where she has special nutritional needs and that can be met with specific nutrients. Claims cannot be made for these conditions, because as discussed earlier, a claim has to have two key components—a substance and a disease. Pregnancy and menopause, although physiologically complex, are not disease states.

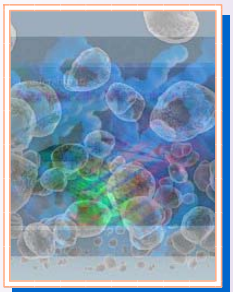
North American women are at risk for certain major nutrition-related diseases and conditions, including diabetes mellitus, cardiovascular disease, several cancers, and osteoporosis, conditions that might benefit from specifically targeted functional foods. Development of gender-based medicine and the growing concerns of women with health issues has led to an increased demand for functional foods as reflected by heightened sales from over $50 billion in 2004 to an anticipated $70 billion by 2009. The marketing of products with a gender in mind is not a novel approach; the "for women only" and "formulated for women's health" segments are reached over $4 billion in retail sales in 2004, up approximately 11 percent from the year before.

Functional foods represent an area that will likely remain of interest to consumers contemplating life-long, beneficial effects from day-to-day nutrition. It is anticipated that in the future, functional foods will be designed for people with special needs, such as those of adolescents, women of childbearing age, athletes, military personnel, the elderly, and people with chronic conditions. The selection process for consumers making choices concerning diet and supplements is complex, which should alert industry and regulators to focus on two key areas—the importance of using sound science when substantiating claims for functional foods, and educating the public to facilitate their decision making.

(Continued from page 1- Nano article)

greatly enhanced. Silver NSPs incorporated into clothing and food wrapping have excellent antibacterial properties. Moreover, in medicine and diagnostics, there is the promise of directed treatment of cancer and other debilitating diseases.

However, the advantages of this promising technology cannot blind us to the potential risks; that is, if basic chemical properties are changed, it should be obvious that interactions with biological systems are changed as well. Concern that there can be a change in the fundamental safety of a NSP has given rise to a new field—nanotoxicology. The possible new effects likely to be observed with NSPs are those that are primarily involved with absorption, distribution, metabolism, and excretion. For example, NSPs can cross the plasma membranes more easily or pass through interstitial spaces (or, so-called "tight junctions"); in some instances, NSPs can pass through virtually impermeable blood-brain and placental barriers. Further, if NSPs are taken up by cells by non-traditional mechanisms or in increased amounts, this is an indication that normal methods of excretion may also be no longer valid. The implication is that humans may become bioaccumulators with an inability to effectively transport or excrete some NSPs.



Another factor to consider is the inherent toxicity of a substance and the effect of its reduction to nanoscale. For example, if the toxicity of a substance is dependent on physical contact with a cell, think about what happens at particle diameters of 10 nanometers or less, when the surface area is exponentially increased compared with an equal mass of the same substance at micro dimensions. Paracelsus' dictum, "*the dose makes the poison,*" might have to be changed to, "*the dose, as a function of the surface area, makes the poison.*"

Lastly, if the physical properties of a substance can be changed, cannot a change also occur in the toxicity of a substance? We already know of examples where just a change in the size or configuration has changed the toxicity of a substance. For example, whereas many types of asbestos are relatively benign, we know that those that produce crystalline needles of certain dimensions, when inhaled, can produce deadly asbestosis or the cancer, mesothelioma. Food also reveals a change in toxicity related to size of constituent molecules. As an example, degraded carrageenan produces cancer in rats whereas non-degraded carrageenan does not. This finding resulted in a regulation specifying that degraded carrageenan must have an average molecular weight greater than 100,000 Daltons. Also, the number of particles in microcrystalline cellulose with a diameter of less than five microns is limited by regulation.

With all of the possible new applications of NSPs, new problems are equally possible, and the new field of nanotoxicology will come of age. At the present time, the generation of NSPs is expensive, and applications are reserved for the industries where returns are highest, and in highly protected environments such as those in the medical and electronics industries. In about five years, however, the cost of producing NSPs will be substantially lower, allowing for their use in the low-margin industries, such as food and agriculture. Such an expansion of nanotechnology will introduce a greater possibility of unintentional exposure of workers in a relatively unprotected work environment, and eventually, exposure of consumers to potentially negative effects of some nanoparticles. This five-year breathing space will give us some time to develop nanotoxicology to determine where potential problems lay in order to ensure the safe application of this new technology.

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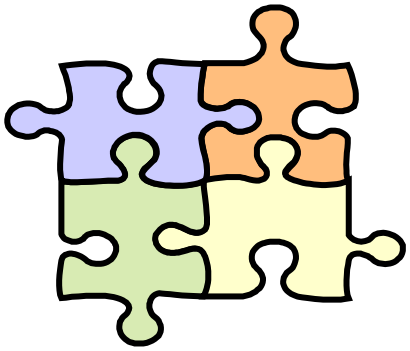

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Burdock **G**roup offers focused expertise to three principal industries:

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Select Pending and Recent Publications

G.A. Burdock, I.G. Carabin and J.C. Griffiths (IN PRESS). **Toxicology and pharmacology of sodium ricinoleate.** *Food and Chemical Toxicology* 44, 1689-1698.

I.G. Carabin. (August 2006). **Functional Foods For Women's Health.** *Natural Products Industry Insider.*

J.C. Griffiths (August 2006). **Adding Antioxidants To Drinks.** *Asia Food Journal.*

P.L. Casterton, D.M. Bagley, W.E. Dressler, H.F. Edelhauser, F.H. Kruszewski, J.P. McCulley, R.B. Nussenblatt, R. Osborne, A. Rothensetein, K.A. Stitzel, K. Thomas and S.L. Ward (2006). **Proposed new classification scheme for chemical injury to the human eye.** *Regulatory Toxicology and Pharmacology* 45, 206-213.

J.C. Griffiths (June 2006). **The Correct Match.** *The World of Food Ingredients.*

B.A. Magnuson (June 2006). **Food allergen labeling: the US Perspective.** *Food and Beverage International.*

For a more in-depth listing of our publications, visit www.burdockgroup.com/publications.html

UPCOMING MEETINGS & SYMPOSIA

September
Council for Responsible Nutrition (CRN)
Annual Symposium On Dietary Supplements
Boston, MA

October
Nano4Food Conference
Atlanta, GA

SupplySide West (SSW)
International Trade Show & Conference
Booth #4076-78
Las Vegas, NV

November
Food Summit
Xiamen, China

Health Ingredients Europe (HI-E)
Frankfurt, Germany

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