BURDOCK GROUP Consultants

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NEWSLETTER
March 2007

Volume 7, Issue 1

NEWS

Dr. George Burdock, President of Burdock Group has been invited to speak at several recent meetings, conferences and Universities.

See page 2 for more details

EVENTS

Come visit us at:
NUTRACON - Supply Expo West
Booth #717
&
SOT ANNUAL MEETING
Booth #1108
See page 2 for more details

OUR COMPETITIVE ADVANTAGES

We are current. We publish.

What has *your* consultant published lately?

Full time, on-site employees

See page 4 for recent publications and visit **www.burdockgroup.com/publications.html**

BURDOCK GROUP'S NEW CLIENT RELATIONS COORDINATOR

See page 3 for more details

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WE SPEAK YOUR LANGUAGE ©
T O X I C O L O G Y!

WE ALSO SPEAK
SPANISH, GERMAN, FRENCH

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Flavonoids

NOVEL FOOD SOURCES AND POTENTIAL HEALTH BENEFITS

By
Sabine Teske, Ph.D.
and
Lonnie Williams, Ph.D.

Today's health-conscientious consumers are constantly in search of the newest "elixir" to fight aging and disease. Consequently, there has been an increased interest in flavonoids, which are antioxidants found in plants that have been suggested to play a role in the prevention of a variety of diseases, including cancer and heart disease. Dietary sources of flavonoids currently in vogue include berries, teas, red grapes, red wine, citrus fruit, onions, parsley, legumes, and dark chocolate. For example, flavonoids in red wine have been linked to the so-called "French Paradox," referring to the relatively low incidence of heart disease among the French population despite a traditionally high-fat diet.

Among berries as dietary sources of flavonoids, acai berries contain a variety of flavonoids, including catechin, epicatechin, cyanidin-3-glucoside, and gallic acid. Ripe acai berries are round, grape-sized, dark purple berries with a single large seed. They grow initially as green berries in bundles on the stems of the *Euterpe oleraceae* palm tree, which is abundant along the swampy river beds of the Amazon River in South America. During July to December, acai berries ripen by turning deep purple, signifying the high content of flavonoids. Compared with other berries such as cranberries and blueberries, acai berries are disproportionately high in antioxidant flavonoids. In fact, the ability of acai berry pulp to scavenge superoxide radicals *via* induction of the antioxidant enzyme superoxide dismutase is considered to be one of highest among fruits and vegetables. As a result of their potent antioxidant effects, acai berries and their products have also been suggested to have anti-inflammatory and anti-carcinogenic potential.

Another interesting herbal source of flavonoids is rooibos tea. It is a fruity, sweet-tasting herbal tea made from the leaves and stems of the rooibos plant (*Aspalathus linearis*), which is indigenous to the mountains of South Africa. Rooibos tea is also referred to as "red tea" because the flavonoids found in rooibos are also pigments that give the leaves and resulting tea a rich, red color. Although rooibos tea is relatively new in the United States, it has been consumed in the Cedarberg mountain region of South Africa for generations. The leaves and stems of rooibos contain high levels of flavonoids, including aspalathin, rutin, and orientin, which have been shown to have significant antioxidant activity. These flavonoids also have been shown to induce apoptosis (spontaneous cell death) of cancer cells, and to reduce DNA damage and lipid peroxidation caused by mutagens in laboratory cultures and in animal studies. Preliminary studies have also suggested that rutin possesses anti-inflammatory activity, strengthens capillaries, and prevents venous edema of the legs due to its antioxidant free-radical scavenging activity. As a result of these studies, the consumption of antioxidants in

(Continued on page 3)

IN THE NEWS...

BURDOCK GROUP EXHIBITS AT TWO CUTTING - EDGE EVENTS

NUTRACON / SUPPLY EXPO WEST EXHIBITION

NATURAL PRODUCTS EXPO WEST

ANAHEIM
CONVENTION CENTER
ANAHEIM, CA

Booth #717
March 9-11, 2007

Burdock Group will be exhibiting at two events during the month of March: ***Nutracon / Supply Expo West Exhibition*** in Anaheim, California and the ***Society of Toxicology (SOT) Annual Meeting*** in Charlotte, North Carolina.

If attending either event, be sure to stop by our booth and say hello; one of our experts can address any questions or issues you may have.

SOT POSTER & PLATFORM PRESENTATIONS

Monday, March 26th

Fumonisin production. Lonnie Williams, Ph.D

Tuesday, March 27th

Pharmacokinetic and developmental safety evaluation studies of methylsulfonylmethane in rats. Ray Matulka, Ph.D.

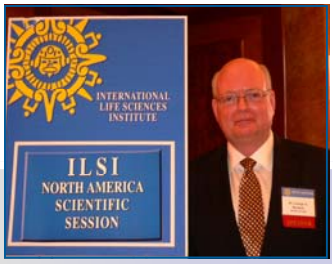
Wednesday, March 28th

D-ribose has non-significant toxicity in both short and long term supplementation. Jim Griffiths, Ph.D.

SOCIETY OF TOXICOLOGY ANNUAL MEETING

CHARLOTTE
CONVENTION CENTER
CHARLOTTE, NC

Booth #1108
March 26-28, 2007



PRESIDENT OF BURDOCK GROUP SPEAKS AT SEVERAL RECENT ENGAGEMENTS

Dr. Burdock has presented at various recent functions including:

- FDA Public Hearing on *Conventional Foods Being Marketed as "Functional Foods"* (Washington, DC)
- ILSI North America Annual Meeting (Cancun, Mexico)
- University of Florida Nutritional Science Department (Gainesville, FL)
- Nutracon/Supply Expo West Nanotechnology work shop (Anaheim, CA)
- University of Mississippi Natural Products Institute and Department of Pharmacology Seminar (Mississippi)

Topics have ranged from *Food Toxicology: An Applied Science*, *Nanotechnology implications for food and food ingredients* and an overview on *Nanotoxicology*.

If you would like to receive a copy of any of the presentations, please contact us at info@burdockgroup.com.

DID YOU KNOW?

✦ **Cardiovascular disease** (CVD) is the largest single cause of mortality among women, accounting for 38 percent of all deaths among females. In the US, 42.1 million (36.6 percent) women live with CVD and the population at risk is even larger. In February 2007, the American Heart Association updated guidelines focusing on women's lifetime heart risk. The new guidelines emphasize the intake of fresh fruits, vegetables and low-fat dairy products, and the decreased intake of saturated fats to less than 7 percent of calories. For omega-3 fatty acid intake and supplementation, recommendations include eating oily fish at least twice a week, and taking a capsule supplement of 850–1000 mg of EPA and DHA in women with heart disease, and two to four grams for women with high triglycerides. Antioxidant supplements (i.e., vitamins E, C and beta-carotene) are no longer used for primary or secondary prevention of CVD and folic acid should not be used to prevent CVD. Guidelines also recommend maintaining a LDL cholesterol of less than 70 mg/dL in very high-risk women with heart disease (which may require cholesterol-lowering drugs). ***www.americanheart.org/presenter.jhtml?identifier=3045524***

✦ You probably heard that it's important to **"drink lots of water."** However, have you ever wondered if it's possible to drink too much? The answer is yes. Drinking too much water can lead to a condition known as *water intoxication* (which in some cases can be fatal) and to a related problem resulting from the dilution of sodium in the body, *hyponatremia*. Water intoxication is usually associated with long distance events like running and cycling. And it's not an unusual problem. For example, water intoxication was reported in 18% of marathon runners and in 29% of the finishers in a Hawaiian Ironman Triathlon in studies published recently in the *Annals of Internal Medicine* and in *Medicine & Science in Sports & Exercise* respectively. ***http://www.hhp.ufl.edu/faculty/pbird/keepingfit/ARTICLE/toomuchwater.htm.***

✦ **Chocolate** is not high in cholesterol. The cocoa butter in chocolate contains stearic acid, which has a neutral effect on cholesterol levels and is not recognized as a source of trans fat. ***www.chocolateusa.org/story-of-chocolate***

✦ A**vocados** are fruits, not vegetables and provide more than 25 essential nutrients, including fiber, potassium, Vitamin E, B-vitamins, and folic acid. ***www.avocado.org/healthy_living/nutrition.php***

NUTRACEUTICALS - WHAT IS THE REAL STORY?

By Shirley-Anne Reul, Client Relations Coordinator

When we hear the term *nutraceutical* bounced around, many of us also think of dietary supplements or functional food. However, the term, which has no meaning in regulations or in the law, was originally conceived in 1989 by Dr. Stephen DeFelice, founder and chairman of the Foundation for Innovation in Medicine (FIM), from the terms "Nutrition" and "Pharmaceutical." According to DeFelice, a nutraceutical can be defined as a "food" (or part of a food) that provides medical or health benefits. A similar term, also with no legal or regulatory definition is *functional food* and is defined by IFT as "foods or food components providing specific health benefits beyond basic nutrition. Then, as today, these terms may only be used for marketing purposes, but may not appear on a label. So what is the difference among dietary supplements, food ingredients, and nutraceuticals or functional foods? *Dietary supplements* are intended to supplement the diet, not replace a meal, and are typically consumed in pill, capsule, tablet, and liquid form. A dietary supplement may not be added to food unless it has also been approved as a food ingredient (i.e., a substance that may be added to food). Any ingredient, whether touted as a *functional food* or *nutraceutical* may only be added to food once it has been approved via a food additive petition or the generally recognized as safe (GRAS) process. And, although added to foods and marketed to imply that it provides some type of health and/or medical benefit, no statement may be made on the label to this effect.

Over the past decade, nutraceuticals have boomed because of the rising costs of pharmaceuticals and the media hype on how wonderful it is to take something referred to as a "natural medicine." But the question to many still remains, "Are they safe?" First and foremost, proven safety of any dietary supplement and/or an ingredient added to food (including nutraceuticals) should be based on its intended use and consumption levels; and, both criteria should have substantiated scientific data to document these safety claims. But, as a consumer, how can you tell? Any new ingredient after October 15, 1994 must abide by the Dietary Supplement Safety Act (DSHEA) by submission of a New Dietary Ingredient Notification (NDIN) to the FDA. Alternatively, because the rejection rate for NDINs hovers around 70%, many manufacturers are opting to go the route of the Generally Recognized As Safe (GRAS) process because the decision on what is safe is taken out of the hands of the FDA. Also, because the GRAS process involves demonstrating safety to the higher standard of "reasonable certainty of no harm," many manufacturers have used this "extra" assurance of a safe product as a marketing advantage.

So, will nutraceuticals continue on their path of being the modern-day way to stay healthy? With billions of dollars spent every year by consumers, and with no slow down in sight, it seems evident that more people are choosing nutraceuticals over pharmaceuticals. However, one thing should be on the top of every person's list when deciding what to produce or consume, and that is "safety first." [1] ***http://members.ift.org/IFT/Research/IFTEExterReports/functional foods_report.htm***

BURDOCK GROUP WELCOMES…

Kerry Drewski as Burdock Group's new Client Relations Coordinator. Stop by to meet Kerry while at Nutracon or SOT - you will be glad you did! Or, you can reach her at kdrewski@burdockgroup.com.

Meanwhile, please join us in wishing Shirley Reul best of luck in her new endeavor!

Kerry Drewski

Preliminary Safety Assessment Without Specific Toxicology Data

By Philip Casterton, Staff Toxicologist

Members of the food industry may hesitate to develop a particular flavoring agent for which they know or suspect there is very little available toxicology information. However, a preliminary safety assessment may still be feasible based on the concept of analogous substances. Although this approach will not take the place of confirmatory animal testing, and is unlikely to be an acceptable method that will gain approvals from the FDA, it can be employed to predict the expected safety of food substances based on their structural similarity to other food substances with established safety profiles. How this concept can be applied is illustrated in the following examples.

Pyrazines constitute a broad family of chemical substances that result from heat-associated non-enzymatic browning of food (generally referred to as the Maillard reaction), which tends to impart earthy, nutty, roasted flavors to cooked foods.

Terpenes constitute a wide-ranging family of flavoring agents that are naturally abundant in botanical species as diverse as fruits, flowers, nuts, and spices to the trees, seeds, stems and roots that yield them. There are countless different naturally-occurring pyrazines and terpenes, many of which can also be manufactured and used to flavor food. Developing a pyrazine substance that has no specific toxicology data may not be a roadblock to further development, though, because the base structural unit of these substances is the pyrazine molecule, which is a weak base. It is known that the gastrointestinal (GI) absorption of weak bases is optimal at pH's that are typical of the intestine (*i.e.*, pH 5–7), so pyrazines are expected to be easily absorbed across the GI epithelium, a phenomenon that also occurs with terpenes due to their lipid solubility. Thus, absorbed pyrazines and terpenes have ready accessibility to the blood where they are transported to the liver and other tissues for further metabolism.

Based on their chemical structure, both substance types are susceptible to biotransformation to substances that will either be excreted in the urine as oxidative metabolites, or further biotransformed by conjugation processes prior to urinary excretion. Therefore, if the expected daily intake of a pyrazine or terpene under development does not exceed the expected safe daily intake of analogous pyrazines or terpenes, it is unlikely that the lack of a complete toxicology data package for a particular pyrazine or terpene would inhibit further confirmatory safety testing that would be expected to support a finding of it being a safe food ingredient. Thus, even though the full-spectrum of desired toxicity of a specific food substance may not be known, its safety may be predicted simply by knowing the chemical structure, assuming that it has a structure similar to a food substance (or substances) known to have acceptable safe daily intake.

In summary, the concept of safety assessment by analogous substances may constitute a valid avenue of preliminary safety investigation for new food substances. However, it is obligatory to understand that the degrees of uncertainty brought by such predictions effectively limit their applicability to one time uses, and even then, are confined to substances that are expected to have intakes below a relatively small exposure such as one milligram *per* day or less.

(Continued from page 1)

rooibos tea has been suggested to prevent free-radical damage that can lead to cancer, heart attack, and stroke in humans; however, many of these health claims are not well documented.

To substantiate health claims associated with rooibos tea and acai berries, further research—in particular human clinical studies—must be conducted. However, in the meantime, rooibos tea and acai berries are continuously gaining popularity in the United States health food and beverage markets. Eventually, these two relatively recent dietary flavonoid newcomers may become more mainstream flavonoid sources as are red grapes and wine.

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WHAT HAS *YOUR* CONSULTANT PUBLISHED LATELY?

Select Recent Publications at Burdock Group

G.A. Burdock and I. G. Carabin (2007). **Safety assessment of myristic acid as a food ingredient.** *Food and Chemical Toxicology* 45, 517-529.

J.C. Griffiths, J.F. Borzelleca and J. St. Cyr (2007). **Sub-Chronic (13 week) Oral Toxicity Study with D-Ribose in Wistar Rats.** *Food and Chemical Toxicology* 44, 155-152.

J.C. Griffiths, J.F. Borzelleca and J. St. Cyr (2007). ***Lack of Oral Embryotoxicity/ Teratogenicity with D-Ribose in Wistar Rats.*** *Food and Chemical Toxicology* 44, 388-395.

R. Matulka, O. Noguchi and N. Nosaka (2006). **Safety Evaluation of a Medium-and Long-Chain Triacylgycerol Oil Produced from Medium-Chain Triacylgycerols and Edible Vegetable Oil.** *Food and Chemical Toxicology* 44 (9): 1530-1538.

G.A. Burdock and S. Teske (February 2007). **The Toxic Potential of Nanotechnology.** *Functional Foods and Nutraceuticals.*

J.C. Griffiths (January/February 2007). **SOY– OH BOY!** *NutraCos.*

J.C. Griffiths (March/April 2007). **Reasonable Expectation of Certainty; How Safe is Safe?** *FDLI UPDATE.*

For a complete list of our publications, visit www.burdockgroup.com/publications.html

UPCOMING MEETINGS & SYMPOSIA

March
Nutracon Nanotoxicology Work Shop
Anaheim, CA

Nutracon/Supply Expo West
Booth #717
Anaheim, CA

Society of Toxicology Annual Meeting
Booth #1108
Charlotte, NC

April
University of Mississippi
Natural Products Institute &
Department of Pharmacology Seminar

This newsletter was prepared by:
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James C. Griffiths, Ph.D.

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