Experts urge a more measured look at antioxidants

In the past decade, antioxidant compounds have gained a reputation among the general public for their ability to mop up reactive and damaging forms of oxygen, often referred to as free radicals. But scientists stress that the testing and commercial regulation of these compounds remains stuck in the past.

The current enthusiasm for antioxidants is perhaps no surprise, given that studies suggesting health benefits from these compounds continue to grab headlines. In April, for example, Jian-Wei Gu of the University of Mississippi Medical Center and his colleagues presented data in San Diego at the annual Experimental Biology conference showing that antioxidants from green tea helped reduce breast tumor size by more than 60% in female mice. The next month, the media focused on findings from a mouse study suggesting that compounds with antioxidant properties might slow the formation of beta-amyloid plaques associated with Alzheimer's disease (*J. Cell. Mol. Med.*, doi:10.1111/j.1582-4934.2008.00344.x; 2008).

The craze over antioxidants gained considerable momentum in the 1990s as a result of large-scale human trials, including a study involving more than 87,000 female nurses that suggested a heart benefit from the antioxidant vitamin E (*N. Engl. J. Med.* **328**, 1444–1449; 1993). Meanwhile, other investigators continue to document how free radicals cause cellular damage and to link these reactive forms of oxygen to illness, including cancer and diseases associated with aging (*Am. J. Cardiol.*, doi:10.1016/j.amjcard.2008.02.006; 2008).

However, many nutritionists now believe that the food store label of 'antioxidant' is quickly becoming the modern day equivalent of snake oil. "You see the pomegranate juices on the shelves that are labeled as super-rich sources of antioxidants that will do these stupendous things for your health," said Edwin Frankel of the University of California, Davis, who has been researching food science for the past 30 years. "But with all the good that the antioxidants will do you compared with all the sugar in the juice, you'd probably be better off drinking a can of Coke."

Yet even though antioxidants have been studied for the last 60 years, much still remains unknown about how the human body absorbs and uses the compounds. Often, products boasting health benefits are largely unsubstantiated in their claims.

For example, antioxidants from whole blueberries have been well documented as promoting brain, cardiovascular and eye function while protecting against cancer. However, processed blueberry juice, such as that found in many popular and expensive health drink cocktails, probably offers dramatically reduced benefits, if any (*J. Am. Pomological Soc.*, **61**, 151–160; 2007).

There are more than 40 established methods for evaluating a food's antioxidant activity, but most rely on measuring chemical reactions under test tube conditions and not on how the compounds actually function in the body. None are officially endorsed by the US Food and Drug Administration, and for good reason, said James Joseph, one of the US Department of Agriculture's foremost antioxidant researchers.

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Dose of reality: Absorption remains unclear

In a recent review of antioxidant studies, Frankel and his colleague John Finley, head of the department of food science at Louisiana State University in Baton Rouge, concluded that even the most popular antioxidant testing methods are unreliable when it comes to predicting how much antioxidant benefit is going to be delivered (*J. Agric. Food Chem.*, doi:10.1021/jf800336p; 2008).

This is because how the body uses antioxidants depends on how those antioxidants are packaged. For example, absorption of antioxidants from green tea and wines has been shown to be dependent on the balance of sugar, fat and ethanol accompanying them on their trip to the small intestine (*Int. J. Vitam. Nutr. Res.*, **77**, 224–235; 2007).

"Comparing antioxidant activity in a test tube with what's going on in the human body isn't comparing apples to oranges—it's comparing apples to ducks," Finley said.

Stu Hutson, Gainesville, Florida

National Cancer Institute helps businesses cross 'the valley of death'

The San Diego–based biotechnology firm NovaRx develops new cancer therapeutics, including experimental approaches involving vaccines. Like many other small companies, NovaRx faces a funding hurdle in advancing drugs from its pipeline into human clinical trials, says executive vice-chairman Habib Fakhrai. In the past, NovaRx has gained support for clinical trials through the US government's Small Business Innovation Research (SBIR) program.

Now, small companies such as NovaRx have the chance to apply for additional financial support from the government to move more cancer drugs into this testing phase: in May, the US National Cancer Institute (NCI) announced that it would devote $10 million annually toward a new initiative known as the Bridge Awards program. The Bridge Awards will complement the already existing SBIR program designed to help small businesses cross the 'valley of death'—the funding gap between the development and commercialization of potentially lifesaving innovations.

Companies applying to the NCI's SBIR program currently compete for several sequential funding phases. The first funding stage establishes the technical merit and feasibility of the proposed research project, and the second and third stages focus on drug development and commercialization, respectively.

Beginning next year, up to ten Bridge Awards—which consist of $3 million given over three years for each project—will help nudge eligible companies from the second to third stage, says Michael Weingarten, director of the SBIR program. "The goal of the awards is to get those cancer drugs and cancer imaging technologies from preclinical development to human clinical trials," he explains. Companies that succeed in securing matching funds from other sources will have an advantage in competing for the Bridge Awards, Weingarten adds.

Prashant Nair, Boston