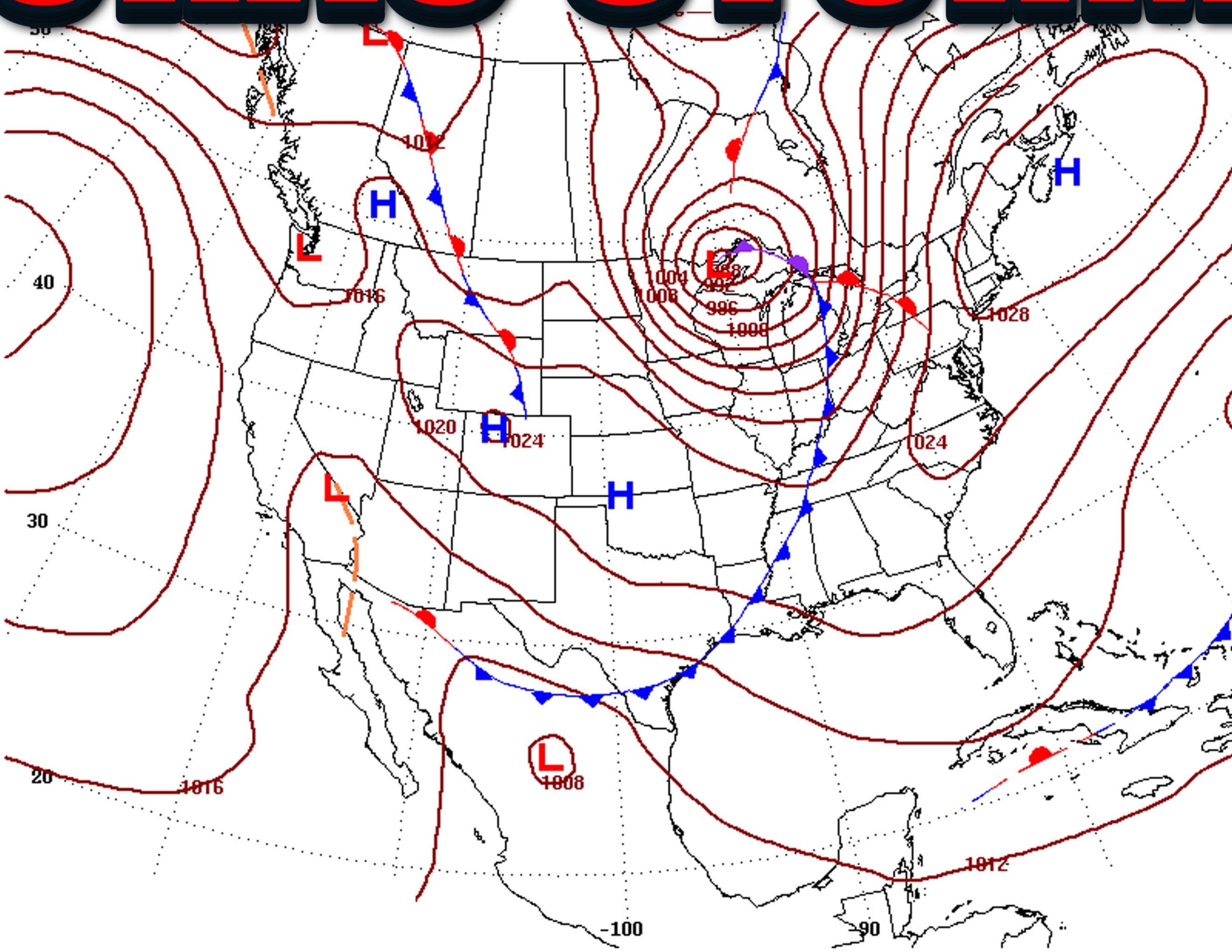
the ORAC STORM



How ORAC 5.0 Has Changed Everything

2013 White Paper, Created by David N. Bell

The ORAC Storm

On May 16, 2012, the Agricultural Research Service ("ARS") of the U.S. Department of Agriculture ("USDA") removed the ORAC database from its website without a full explanation of why they did so. This appeared, to certain skeptics, to be a major change in direction for the department and its main research arm which had actually contributed to the development and widespread use of ORAC for a decade. Furthermore, the Agricultural Research Service had even maintained a database that was considered to be the central repository of reliable ORAC information.

This unexpected decision by the Agricultural Research Service had an immediate and powerful effect on the nutrition industry. To make matters worse, main stream media outlets mistakenly reported that ORAC was now meaningless. These "half-truth" reports confused nutritional companies across the country. Those who once touted the effectiveness of ORAC, now wondered what to do and how they would quantify their health products nutritional-values moving forward. So, what really happened?

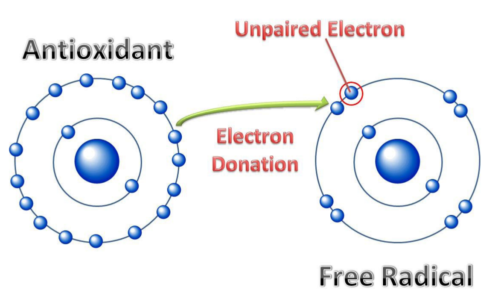
My name is David Bell. I am a Wharton-educated nutritional products expert. My company, Bell Advisory Services (New Bedford, MA), provides critical research findings to food and nutrition industry clients across the globe. Bell Advisory is recognized as an authority on ORAC and antioxidants (aka: AOX). The purpose of this "White Paper" is to provide the facts regarding:

1 - The Truth About ORAC
2 - Why Antioxidants are Vital
3 - ORAC 5.0 – the New Generation
4 - The Future of AOX (i.e. Antioxidants)

What Happened to ORAC and Why? What is the Truth about ORAC?

Definitions: ORAC is an in vitro chemistry method that was developed initially by U.S. government labs and then for "commercial use" by Brunswick Labs. Its purpose is to provide quantitative analytical information about the ability of foods and other sources to absorb, or quench, free radicals. This is a task ORAC has performed admirably.

Radicals are unpaired electrons that are unstable and highly reactive. They bond with other molecules. While radicals are necessary for a number of normal processes in humans, they can also be harmful. When too many are formed in our bodies, they contribute to oxidative damage, or oxidative stress, which is implicated in a wide range of diseases including cancer, stroke, diabetes, high chole sterol, high blood pressure and heart attack.



SOURCE: National Institute of Health
SOURCE: Wikipedia

Confusion further spiked when conflicting actions arose between notable organizations. While the Agricultural Research Service ("ARS") pulled down its ORAC data, just this year the AOAC (a respected international standards organization) approved ORAC as a First Action Official Method for testing antioxidants in foods. In its announcement, AOAC stated that,

> *"The ERP agreed that the method provides good information, particularly on the analytical range and LOD (limits of detection). The method is applicable to several different foods, covering a wide range of matrixes."*

It is valuable to note that the Expert Review Panel at the AOAC that recommended ORAC for approval was actually chaired by James Harnly, a USDA scientist.

SOURCE: Natural Products Insider
SOURCE: ORAC Database 1st Action Method
SOURCE: Bio-Medicine.org

Despite these contradictions at the USDA, the fact is, ORAC was and remains a valid, valuable analytical method. ORAC is recognized by nutritional researchers and consumer products companies alike as the most reliable resource to measure AOX. However, as with any tool, logically there are a few important limitations to it. Like any other "in vitro" chemistry method, when used to test food samples, ORAC does not provide individual information about outcomes in human health. However, it does provide accurate data to form population generalities.

For example, if you had a box of Xocai (a high-antioxidant dark chocolate product line) and you looked at the Nutrition Facts label on the back of the box, you would see some interesting data there. See that number for, Soluble Fiber or Vitamin A? Both of those results were measured with "in vitro" chemistry methods (i.e. ORAC). Although neither, by itself, tells us anything about the benefits of fiber or vitamin A to human health, these numbers do provide us with the most dependable "in vitro" nutritional data that is available to science. It is the job of clinical investigation to establish links between nutrition consumption and health outcomes.

SOURCE: Wikipedia
SOURCE: Dr. Weill

ORAC has, however, been instrumental in guiding investigative research about the benefits of antioxidant foods. It is the premier method for quantifying antioxidant potential of food sources, and plays a major role in guiding clinical investigation as a trusted measure of antioxidant intake. We will explore this in detail, below.

ORAC – Common Misconceptions

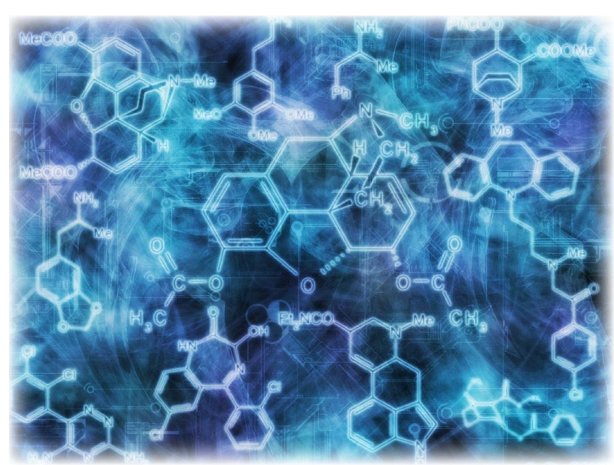
Before we dive into recent clinical research that supports the use of ORAC, let's clear up a few common misconceptions about ORAC.

The FDA and ORAC. The U.S. Food and Drug Administration ("FDA") is responsible for protecting public health in part by regulating foods, supplements, and drugs. An important function is the regulation of food labeling, which includes items that must be, can be, and cannot not be included on a food or supplement label.

Misconception #1: The FDA does not approve of ORAC. As a valid method, ORAC is allowed by the FDA as a unit of measure on food and supplement labels. However, there are two major types of label claims that the FDA does not allow in connection with ORAC.

Misconception #2: The FDA has singled out ORAC-based health and/or disease claims. The FDA, as well as other regulatory agencies around the world, requires that health and/or disease claims be substantiated by a body of clinical evidence. According to the FDA, this connection has not been established between ORAC and specific health or disease claims. This is also true for most other ingredients or performance characteristics. ORAC is in good company: health and disease claims are hard to come by. However, as we will see, there is a large body of clinical research that establishes the relationship between ORAC and human health.

Misconception #3: The FDA Prohibits use of the term "Antioxidant" on labels. The FDA has a terminology restriction that is commonly misunderstood. On food labels, it only allows the use of the term "high" in antioxidants in relation to those nutrient antioxidants for which a Recommended Daily Intake (RDI) have been established. In FDA thinking, the term "high" only has relevance in relation to an established unit of measure: That unit is an RDI. To date, only vitamins A, C, E, beta-carotene (as a source of vitamin A) and the micronutrient selenium have RDIs. However, this limitation does not apply to valid quantitative methods – including ORAC. This labeling restriction often leads to the mistaken opinion that the FDA prohibits use of ORAC on labels; it does not.



SOURCE: www.fda.gov

SOURCE: www.fda.gov

Clarification: Now, this FDA regulation does not mean that, say, polyphenols (like cocoa flavanols) are not antioxidants. Research clearly demonstrates that they are. It simply means that the FDA has not yet established an RDI for cocoa flavanols as a source of dietary antioxidants. Coincidentally, the FDA has not established a RDI for ORAC either. In reality, however, the FDA may not add RDIs for nutrient antioxidants in the foreseeable future. This is a deficiency in regulatory politics, not antioxidant science. In the meantime, for example, Xocai dark chocolate products provide responsible, quantifiable information about ORAC and flavonoid content. The data from Xocai is consistent with FDA regulations and they proactively assist consumers make informed decisions about their nutrition purchases.

Conclusion: The take-away. Responsible use of valid ORAC results, such as Xocai's presentation of ORAC values, is allowed by the FDA and, as we will see, also provides valuable guideposts for the informed consumer.

How Much ORAC Should We Consume?

We know that the FDA has not established an RDI (i.e. Recommended Daily Intake) for ORAC. So, is there any guidance on dietary intake of ORAC and potential health benefits?

A recent study provides invaluable information on both:

- ✓ The connection between antioxidant-rich diets and human health outcomes, and
- ✓ The levels of ORAC in foods that are related to these health outcomes.

The study was performed by Ronald Prior and colleagues. Dr. Prior was the director of the USDA antioxidant research program for over 20 years and was a leading figure in the development of the ORAC assay. He is an expert in the antioxidant role of polyphenols.

SOURCE: http://www.nwpii.com/ajbms/papers/AJBMS_2013_2_03.pdf

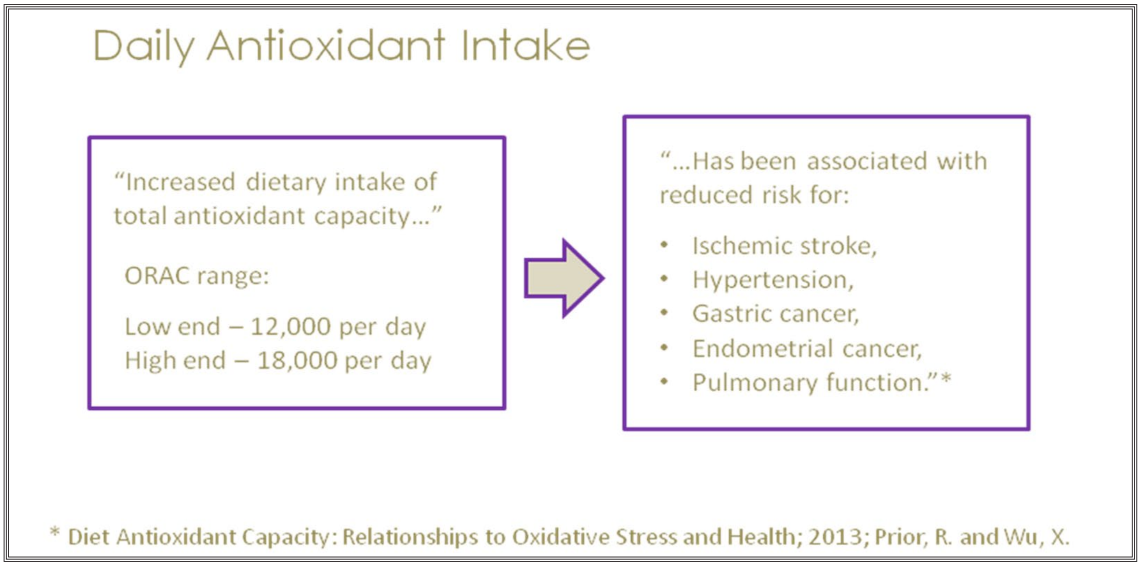
The Prior et. al. peer-reviewed article provides a comprehensive review of human clinical research that encompasses small, medium, and large-scale studies and, in aggregate, thousands of subjects.

For example, the Mayo Clinic Case-Control study reviewed 603 cases and 1,007 controls; the Singapore Chinese Health Study contained more than 63,000 women and men 45-74 years of age; and the Swedish Mammography Cohort analyzed 32,561 subjects in a long-term epidemiological study.

MAYO CLINIC

What did Dr. Prior and his esteemed colleagues find? Their research found that an antioxidant-rich diet, as measured by ORAC, had a range of significant beneficial health outcomes. Some of these are described in the exhibit below.

Exhibit 1

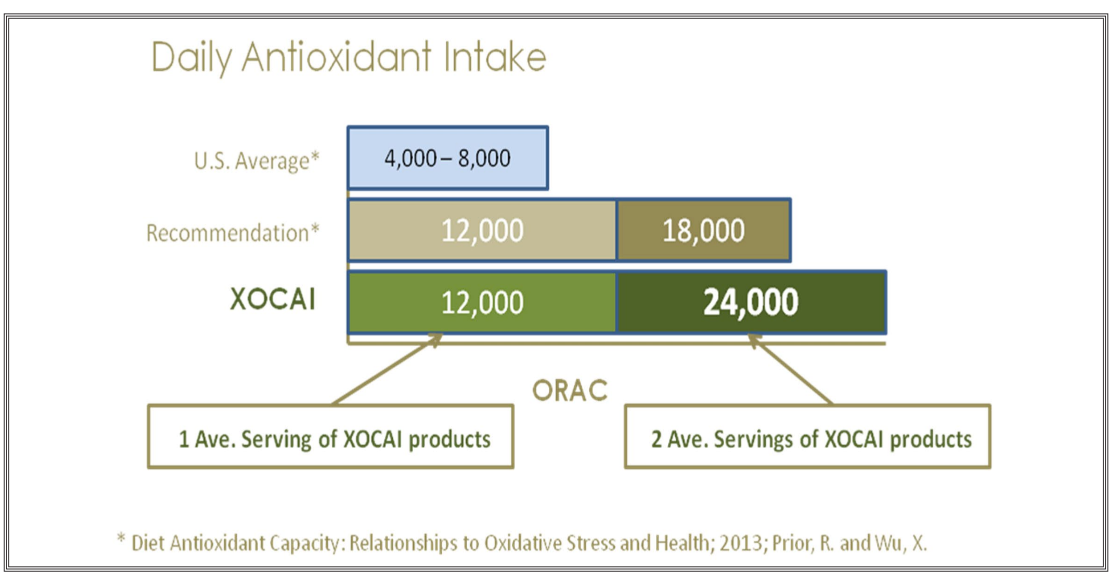


This peer-reviewed study clearly establishes a range of daily ORAC intake that is associated with long-term health outcomes. It shows that diets associated with reduced risk of disease include foods that provide a level of antioxidants that correspond to ORAC values of between 12,000 and 18,000 per day.

Dr. Prior's study also examines the ORAC levels below which healthful benefits are not observed. It is not surprising that, based upon USDA dietary intake data, the average U.S. consumer's daily ORAC intake is not sufficient to achieve those benefits. In fact, his research indicates that in the U.S., the average person's diet consists of between 4,000 and 8,000 ORAC value from food sources.

Let's see how well the heretofore mentioned Xocai dark chocolate products meet this new standard. The exhibit, below, shows the study's findings along with Xocai products average ORAC contribution.

Exhibit 2



Conclusions: On average, a single serving of one of Xocai's dark chocolate products satisfies the minimum antioxidant dietary intake found by Dr. Prior's study to support beneficial health outcomes, and two servings per day exceeds the upper range in the study.

SOURCE: Xocai ORAC
SOURCE: USDA

About MXI Corp: Established in 2005, Marketing Xocolate International Corporation (MXI-Corp) is the world leader in great tasting, healthy, dark, chocolate products. All MXI products are focused on potent doses of delicious, antioxidant-rich Belgian cacao. MXI-Corp believes that the high levels of natural antioxidants and Polyphenols that are found in its cacao can provide a viable solution to individual nutritional needs. The Xoçai™ (sho-sigh) line, which currently includes nine products, is manufactured utilizing a cold-press process, which preserves the nutritional values of the company's proprietary blends of vitamins and minerals.

A Sidebar about "Raw Foods"

I am frequently asked about whether or not raw foods are preferable to processed ones. While this could be the topic of its own paper, the short response is that there is no simple yes or no answer. Let's look at some of important considerations.

1) Nutrient benefit. Some processes may damage nutrient benefits, others may improve them. The outcome is dependent upon both the process and the food source. For example, alkalizing of cocoa reduces antioxidant capacity, but the cooking of tomatoes can increase bioavailability of antioxidants.

2) Preservation of food quality. There is no doubt that consumption of fresh foods is a valuable dietary practice. However, there is also an important role for stable foods – foods that preserve nutrient benefits over time. This is more difficult to accomplish with raw foods than with processed foods.

3) Reliability. Raw foods can vary widely in nutrients such as antioxidants. Even your favorite variety of apple may have a variation of greater than 30% depending upon its source, age, or other factors. Also, most consumers waste as much as 25% of the fresh produce they purchase due to spoilage.

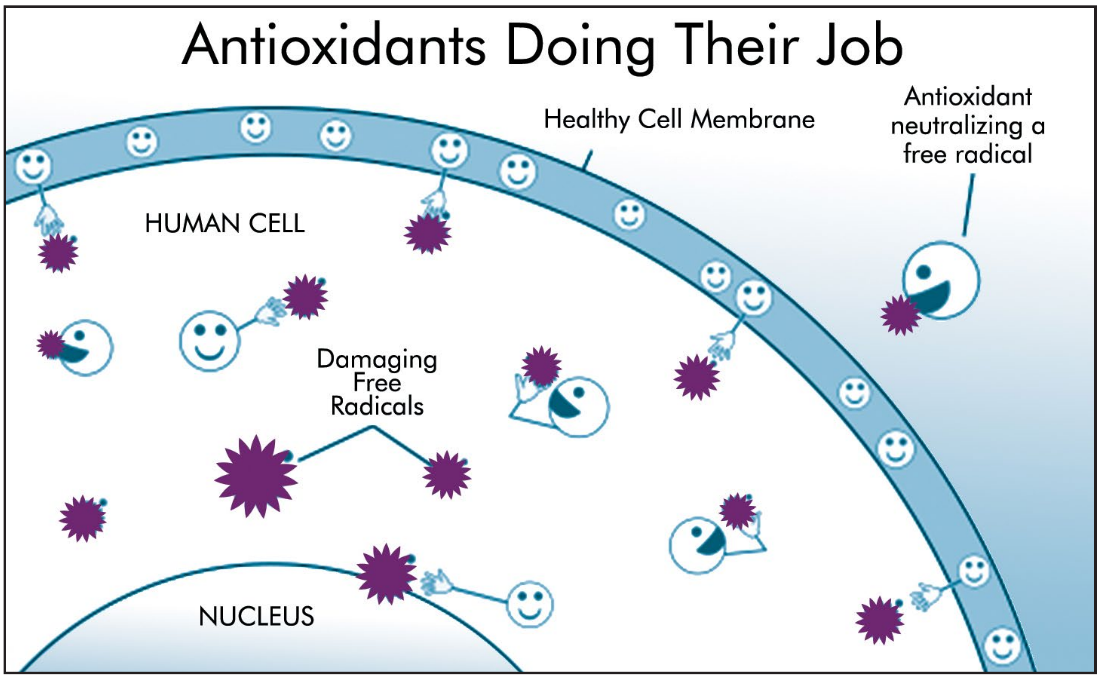
In short, there is a great value to foods like Xocai products that provide proven, consistent, stable nutrient benefits in every serving.

SOURCE: Xocai Research
SOURCE: Xocai Chocolate and Weight Loss
SOURCE: Xocai Cacao
SOURCE: Regular Chocolate vs. Healthy Chocolate

The Next Generation – ORAC 5.0

Several thousand polyphenolic compounds exist in plants and many of these have antioxidant capacity (AOC). Because of the difficulty of quantitating the individual antioxidant compounds, a method which provides a "sum" of the antioxidant components in plants and biological samples is useful.

These types of assays are often referred to as "total" antioxidant capacity assays. However, there is in actuality no single assay which provides a "total" measurement of antioxidant capacity. In thinking about antioxidant capacity methods, one has to consider the oxidant source and the mechanism of reaction with potential antioxidants. Experimental evidence has suggested that there are six major reactive oxygen species (ROS) causing oxidative damage in the human body. These species include: superoxide anion (O2·-); hydrogen peroxide (H2O2); peroxyl radicals (ROO·); hydroxyl radicals (HO·); singlet oxygen (1O2); and peroxynitrite (ONOO-).



The peroxyl radical is the most abundant free radical in the human body. Another one of the more relevant radicals in biological regulation is superoxide anion radical. The superoxide anion is formed by the reduction of molecular oxygen in the process of energy metabolism.

While ORAC represents antioxidant capacity against one type of free radical, the peroxyl radical, there are four other primary radicals at work in our bodies damaging our cells and tissues as well. They include: hydroxyl, peroxynitrite, superoxide anion, and singlet oxygen radicals. These radicals each behave differently and can require different kinds of antioxidants to combat and neutralize them, just as viruses require different antibiotics to eradicate their activity.

SOURCE: Wikipedia

In short, broad-spectrum antioxidant protection is necessary to address this host of radicals. This is the goal of ORAC 5.0., which was developed to measure the antioxidant effect of foods on all five primary radicals. Xocai's Brunswick Labs Certified ORAC5.0 performance demonstrates trusted, comprehensive antioxidant protection against these five primary radicals.

SOURCE: Brunswick Labs

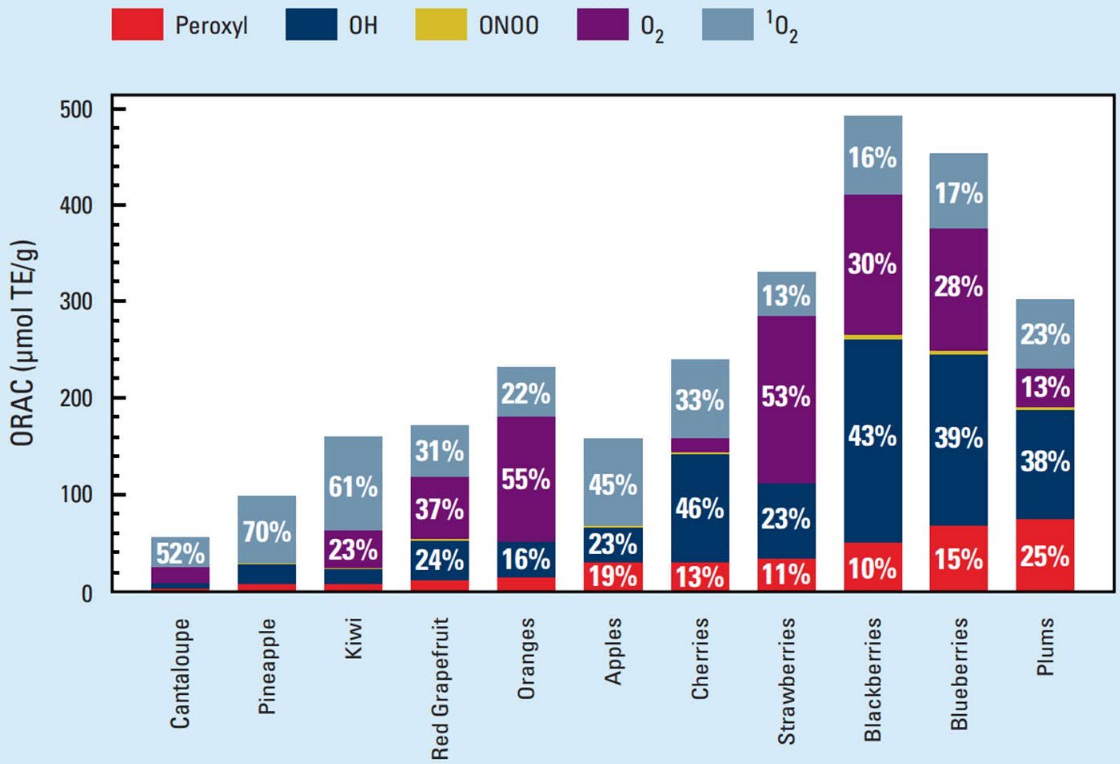
Accumulated evidence indicates that reactive oxygen species, such as peroxyl radicals (ROO·), hydroxyl radicals (HO·), the superoxide anion (O2-·), and singlet oxygen (1O2), are involved in the pathophysiology of aging and a multitude of diseases. To counteract the damage of the reactive oxygen species on living cells, a defense system is designed biologically to neutralize the reactive oxygen species or to prevent the reactive oxygen species from being generated in the first place.

Depending on the reaction mechanisms, antioxidants are often classified into two major categories: radical chainbreaking antioxidants and preventive antioxidants. Chainbreaking antioxidants convert reactive free radicals (e.g., HO·) to stable and thus nonaggressive molecules through hydrogen atom transfer reactions between HO· and the antioxidants. As a result, the autoxidation chain reactions between the free radicals and the cellular molecules are terminated.

Preventive antioxidants inhibit the oxidation reaction from occurring by either converting the precursors of the reactive oxygen species to unreactive species or inhibiting the oxidation reaction. To counteract the assault of the superoxide anion reactive species, living cells have a biological defense system composed of enzymatic antioxidants to convert reactive oxygen species or reactive nitrogen species to harmless species. In contrast, no enzymatic action is known to scavenge ROO·, HO·, 1O2, and ONOO-, so the burden of defense relies on a variety of non-enzymatic antioxidants such as vitamin C, and vitamin E, and many phytochemicals that have the property of scavenging oxidants and free radicals.

To comprehensively evaluate the oxidant-scavenging capacity of a food sample, assays have to be designed to include these reactive oxygen species. However, so far the majority of assays are designed to measure a sample's capacity to react with one oxidant (either organic radical or redox active metal complex). The peroxyl radical has been the most frequently used reactive oxygen species in antioxidant capacity assays because it is the most relevant radical in lipid autoxidation and can be generated conveniently from azo compounds. The peroxyl radical has been used as a radical source in the Oxygen Radical Absorbance Capacity (ORAC).

Figure 1: Radical Source and Antioxidant Capacity of Fruits

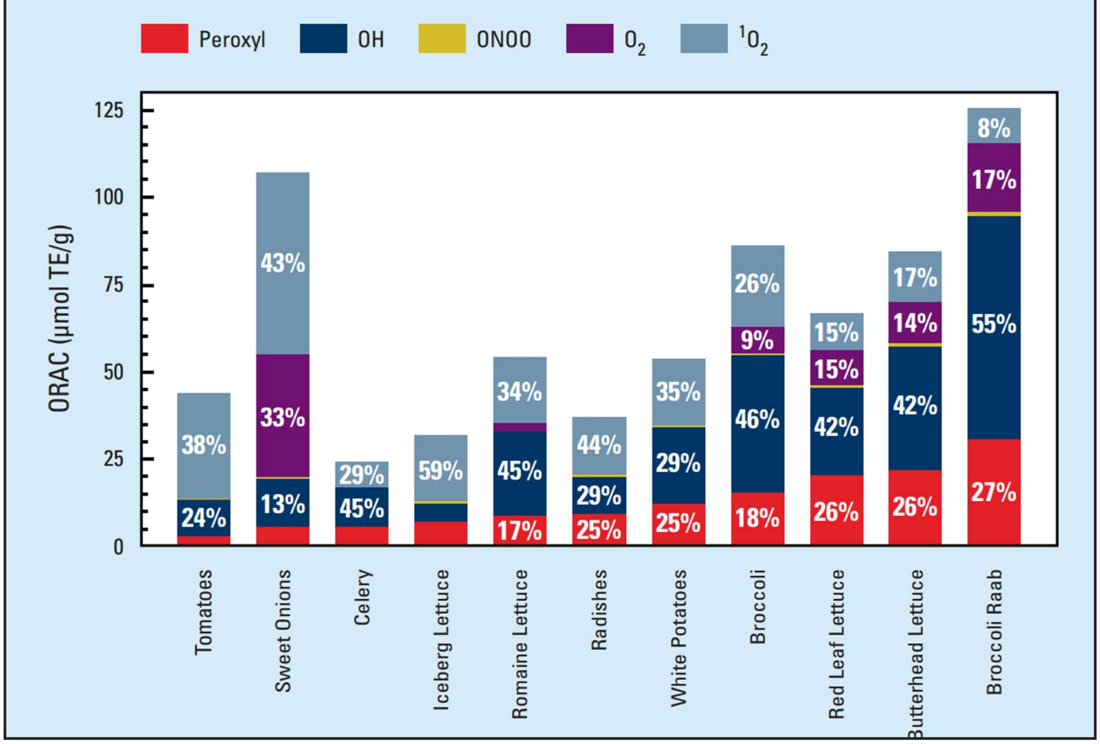


It is evident that the antioxidant defense “team” in living cells contains individual antioxidants that function in very different tasks in the battles against oxidative stress and reactive oxygen species. Therefore, it is imperative that to comprehensively evaluate the antioxidant capacity of food nutrients in vitro, we need a broad range of assays that can cover all aspects of antioxidant capacity. It is impossible to have a one-fits-for-all assay. Although there is a validated assay for peroxyl radical absorbance capacity (ORAC) (1-5), no such assay had been developed for any other of the reactive oxygen species, until Brunswick Laboratories first published methods for the analysis of antioxidant capacity using the hydroxyl, and superoxide anion radicals (6, 7).

Brunswick Laboratories has subsequently addressed the other oxygen radical species [singlet oxygen (1O2); and peroxynitrite (ONOO-)] by developing assays that assess their contribution to total antioxidant capacity.

A sample of available data is presented in Figure 1 and 2 on fruits and vegetables. From this data, it is evident that there is little or no correlation among the different radical sources used to assess antioxidant capacity.

Figure 2: Radical Source and Antioxidant Capacity of Vegetables



One example that stands out is with tomatoes, which has a very low antioxidant capacity as measured with the peroxyl radical, but much higher antioxidant capacity using the singlet oxygen radical (Figure 2). Furthermore, the original peroxyl ORAC represents no more than 27% of the antioxidant potential of selected fruits and vegetables. The other radical assays added to the ORAC suite represent the preponderance of antioxidant potential.

Addendum 1 - Brunswick Labs Content

By measuring all primary reactive oxygen species, ORAC5.0™ provides new opportunities which can be used in the formulation of nutritional products that deliver quantifiable, maximal protection against multiple radical sources.

Finally, research shows that oxidative stress caused by free radical activity can trigger a cascade of other harmful effects. In fact, Jeffrey Blumberg, PhD, Director, Antioxidant Research Lab, USDA, has said that the most important health implications of most antioxidants may not be their capacity for direct radical quenching, but, rather, their broader mechanisms of action. These include protection against systemic and localized inflammation, support of healthy immune response, protection of collagen and elastin in the skin, stimulation of metabolism, and more.

In pre-clinical cell-based tests, Xocai demonstrates significant efficacy in inhibiting the inflammatory marker, NFkB, and stimulating the metabolic marker, SIRT1.

SOURCE: Brunswick Labs
SOURCE: Brunswick Labs
SOURCE: http://clinicaltrials.gov/ct2/show/study/NCT00666250?show_desc=Y#desc

Q&A: ORAC5.0 and Why All 5 Radicals Matter

Key Points:

- There are a variety of "free radicals" that operate in humans – the most important of which are the primary radicals hydroxyl, peroxyl, peroxynitrite, singlet oxygen, and superoxide anion
- These radicals are formed, behave, and are defended against differently
- They all contribute to (1) a general condition called "oxidative stress," or cellular damage, and (2) broad human health concerns caused, for example, by inflammation, DNA and protein damage
- They are each implicated in different health problems – from cardiovascular disease to macular degeneration and Alzheimer's disease
- They are directly linked to skin damage and aging

Q: Is peroxyl the most important radical, or the one that best measures antioxidant capacity?
A: While peroxyl is an important radical, and was as good a starting spot for developing a single ORAC assay, it is not more important than the other primary radicals. From a commercial standpoint, it was first to market and has gained use and recognition.Brunswick Labs has always stated clearly that peroxyl ORAC is a representation of antioxidant capacity; it does not measure complete or comprehensive antioxidant capacity; it is not a "universal" antioxidant measurement.

Q: What do you mean by "universal" measurement?
A: We mean that peroxyl ORAC favors certain antioxidants that work better against the peroxyl radical. For example, compounds such as anthocyanins in the flavonoid family quench peroxyl better than compounds such as lycopene in the carotenoid family.

Q: Why should I test against hydroxyl or other radicals?
A: For the same reason that a health checkup measures blood pressure, cholesterol, PSA (for men), and a mammogram (for women). The following descriptions demonstrate the important differences between the radicals and their roles in human health concerns.

Premium antioxidant products are often a complex matrix of compounds that come from diverse natural sources. Such products are likely to have broad-spectrum antioxidant potential and are ideally suited to Total ORAC5.0.

Q: Can you describe how the other radicals are different from peroxyl?
A: Hydroxyl. Hydroxyl is highly reactive and cannot be eliminated by our endogenous enzymes (such as SOD and glutathione). It can damage virtually all types of acromolecules: carbohydrates, nucleic acids, lipids, and amino acids. In the skin, hydroxyl radicals are created by UV exposure.

Peroxynitrite. Peroxynitrite is a reactive nitrogen species that is particularly harmful to proteins. It has been implicated in the development of certain cancers, hepatitis, and chronic inflammation. In the skin, peroxynitrite contributes to the breakdown of vital proteins, such as collagen.

Singlet Oxygen. In the skin, singlet oxygen is generated by UV. In vivo, it is linked to the oxidation of LDL cholesterol and cardiovascular disease. Singlet oxygen is highly unstable and durable. Carotenoids are very effective at scavenging singlet oxygen.

Superoxide anion. Superoxide anion is a precursor of all other reactive oxygen species – sometimes referred to as “the mother of free radicals.” It is highly toxic and contributes to lipid and DNA damage. Antioxidants that scavenge superoxide anion also help prevent the formation of radicals such as hydrogen peroxide and hydroxyl. Superoxide anion has been linked to hypertension and cardiovascular damage.

SOURCE: Brunswick Labs

Addendum 2 - Brunswick Labs Content

Xocai Delivers

So what can we conclude? Here is a summary review:

- ORAC is a valid, industry-approved method for measuring antioxidants in foods
- An antioxidant-rich diet contributes to good health
- ORAC5.0 describes broad-spectrum antioxidant protection against five primary radicals
- Broad-spectrum antioxidants also perform other mechanisms of action, such as anti-inflammatory and pro-metabolic functions

Xocai dark chocolate products deliver, providing certified superior antioxidant protection in every serving.

About David N. Bell

David N. Bell is a highly respected food and nutrition advisor. He has worked with major companies in industry for almost 40 years. Bell is recognized by industry organizations and companies as a leading authority on antioxidants in consumer products.

Bell began his career with Ray A. Goldberg at Harvard Business School where he worked with some of the most creative and influential minds in the global food industry. He began Bell Advisory Services in 1991 and has worked with international corporations, entrepreneurs, and companies in all parts of the food and nutrition industry. Today, Bell Advisory is a respected business which has served over fifty clients.

Bell has been an advisor to Brunswick Labs for many years. He has played a primary role in commercializing the ORAC and ORAC5.0 programs, and in increasing industry awareness about the versatile role of food-based antioxidants. In this capacity with Brunswick Labs, Bell has helped establish the concept of nutrient "super foods," including acai, cocoa, and many others.

A central part of Bell's work is the application of leading-edge science to the analysis and understanding of natural products. In this capacity, Bell has directed a wide range of investigative studies – from ground-breaking characterization of novel food sources to human clinical studies. Bell has worked in conjunction with the USDA, The Harvard School of Public Health, and Johns Hopkins University and has provided clinical guidance and professional advice for leading global companies, including Glaxo Smith Kline, Nestle, Kraft, and Procter & Gamble.

Bell is also known for providing value to companies by translating good science into a consumer vocabulary. In this role, Bell has given presentations around the world and helped spread a consumer understanding about natural products, antioxidants, and human health.

As an advocate for high-antioxidant products, Bell naturally was intrigued by MXI Corp's mission and drawn to their Xocai Healthy Chocolate product line (circa 2005). Bell has enjoyed the relationship with Xocai, having directed multiple analysis projects of Xocai chocolates (i.e. Cell-Based ORAC investigations). He has also had the honor of presenting the clinical results of these studies at MXI Corp Annual Conventions. Bell has regularly expressed his admiration for the innovative and responsible industry leadership demonstrated by MXI Corp – qualities that are reflected in its superior products.

REFERENCES

1. Cao, G.; Prior, R. L., Measurement of Total Antioxidant Capacity in Nutritional and Clinical Studies. In Handbook of Antioxidants, Cadenas, E.; Packer, L., Eds. Marcel Dekker, Inc.: New York, 2001; pp 47-55.

2. Ou, B.; Hampsch-Woodill, M.; Prior, R. L., Development and validation of an improved oxygen radical absorbance capacity assay using fluorescein as the fluorescent probe. J. Agric. Food Chem. 2001, 49, 4619-4926.

3. Huang, D.; Ou, B.; Hampsch-Woodill, M.; Flanagan, J.; Prior, R. L., High-Throughput assay of oxygen radical absorbance capacity (ORAC) using a multichannel liquid handling system coupled with a microplate fluorescence reader in 96-well format. J. Agric. Food Chem. 2002, 50, 4437-4444.

4. Prior, R. L.; Hoang, H.; Gu, L.; Wu, X.; Bacchiocca, M.; Howard, L.; Hampsch-Woodill, M.; Huang, D.; Ou, B.; Jacob, R., Assays for hydrophilic and lipophilic antioxidant capacity (Oxygen Radical Absorbance Capacity (ORACFL)) of plasma and other biological and food samples. J. Agric. Food Chem. 2003, 51, 3273 -3279.

5. Wu, X.; Beecher, G.; Holden, J.; Haytowitz, D.; Gebhardt, S. E.; Prior, R. L., Lipophilic and hydrophilic antioxidant capacities of common foods in the U.S. J. Agric. Food Chem. 2004, 52, 4026-4037.

6. Ou, B.; Hampsch-Woodill, M.; Flanagan, J.; Deemer, E. K.; Prior, R. L.; Huang, D., Novel fluorometric assay for hydroxyl radical prevention capacity using fluorescein as the probe. J. Agric. Food Chem. 2002, 50, 2772-2777.

7. Ou, B.; Huang, D.; Prior, R. L.; Hampsch-Woodill, M.; Flanagan, J. A. In A high throughput assay for superoxide radical absorbance capacity (S-ORAC) of botanicals, First International Congress on Antioxidant Methods, Orlando, FL, 2004; Orlando, FL, 2004.

NOTES