Nutrient of the Month: Quercetin

How many decades ago did moms start encouraging their kids to eat the white part of inner citrus peels because they contained flavonoids? Plants produce quercetin, a major flavonol, in response to light (especially ultraviolet), so leaves and peels tend to be good sources: onions and onion skins, apples and apple peel, black and oolong tea, red wine, berries, garlic, shallots, turmeric, peppers, and the leaves of evening primrose and hypericum are generous providers. While quercetin bioavailability is generally low, transformation by gut bacteria such as *Bifidobacterium adolescentis* may mediate or amplify effects of flavonoids. Early research even suggests that quercetin may improve microbiome composition and limit the growth of species associated with diet-induced obesity and dysbiosis. Though many laboratory studies have focused on understanding the effects of single flavonoid entities, research on food extracts and flavonoid blends often find that combinations convey greater benefit, as different species show complementary effects.

Quercetin is well-recognized for its impressive resumé of antioxidant qualities, but its influences on cellular and mitochondrial aging processes and inflammation may be even more compelling:

--In only 2 weeks, 1 gram/day quercetin improved young men’s treadmill exercise performance and modestly increased markers of muscular mitochondrial biogenesis, including sirtuin 1 (Sirt1) and PGC1α (PPARγ coactivator 1α) gene expression

--Quercetin has displayed several anti-mutagenic and -carcinogenic mechanisms:
  o inhibit telomerase activity (which helps preserve DNA structure)
  o limit bioactivation of some mutagens
  o interact with signaling systems involved in carcinogenesis and cell death
Quercetin activates sirtuin 1 (Sirt1), one of the prime regulators of cell life/death cycles and creation of mitochondria.

Flavonoids including quercetin safeguard DNA integrity against oxidative damage through chelation.

In animals with high-fat diet-induced inflammation and insulin resistance, quercetin:
- shifted macrophages away from the more pro-inflammatory M2 polarization towards "housekeeping" M1 expression and reduced recruitment of mast cells in adipose tissue.
- rescued Sirt1 genetic expression and signaling of AMPK (AMP-activated protein kinase, a critical controller of the cellular energy economy)—partly through direct activation.
- partially normalized insulin, leptin, and adiponectin levels and improved insulin sensitivity and glucose uptake while reducing gains in weight and body fat.
- lowered blood and adipose levels of key inflammatory markers IL-6, TNFα (tumor necrosis factor-α), and MCP-1 (monocyte chemoattractant protein-1).
- attenuated visceral and hepatic fat accumulation and improved expression of genes related to lipid metabolism (PPARγ and SREBP, sterol regulatory element-binding protein).

In men and women with elevated blood pressure, quercetin improved markers of endothelial dysfunction and inflammation, and in a high-glucose environment, quercetin helped preserve endothelial cell function by preventing PARP (poly-ADP-ribose polymerase, involved in DNA repair and cell death) overactivation and sparing cellular energy (as NAD, nicotine adenine dinucleotide).

In animals with homocysteinemia induced by excessive methionine intake, improved remethylation and transsulfuration of homocysteine of homocysteine and thereby lowered levels.

Quercetin is also known for aiding T-helper 1 and 2 (Th1 and Th2) immune response balance, radical scavenging, protection against a wide range of reactive oxygen and nitrogen species (ROS and RNS), limiting production and genetic expression of inflammatory mediators, antiviral activity, and inhibiting lipid peroxidation and histamine release. An animal study involving peanut allergy suggests that quercetin may even protect against some IgE-mediated allergy and atopy. A recent preclinical study found that it helped re-establish equilibrium between T-regulatory and T-helper 17 cell populations, which in imbalance are implicated in some autoimmune conditions.

Mom was, of course, right—it really is worth it to find some way to consume those (preferably organic) peels and skins—whether directly or by brewing up some tea or broth with them!

2018 Thought Leaders Consortium Preview: Methylation

Methylation. It's a topic that prompts questions, conversation, and even controversy. Watch this video to learn more about the methylation discussion that will take place at PLMI’s Thought Leaders Consortium next month. Limited seating is still available, but registration will close October 5, 2018.

Video Link: https://vimeo.com/289780023

The Sixth Annual Thought Leaders Consortium
Resource Spotlight: The Mother of Metabolic Network Diagrams

Do you sometimes search for the name of a particular metabolite or metabolic pathway—or perhaps new research has updated knowledge since you last cracked open your biochem texts anyway? Do you sometimes wish you had one of those great charts that take up entire walls but depict all those networks? The Kyoto Encyclopedia of Genes and Genomes, also known as KEGG databases, can provide this information for you by generating organism-specific metabolic pathway diagrams at different levels of hierarchy. The opening page gives a 35,000-foot view comprising pretty much everything—metabolism of amino acids, lipids, carbohydrates, vitamins/cofactors, glycans, antioxidants, nucleotides, carbon, nitrogen, sulfur, antibiotics, xenobiotics, and more—and you can click on different areas of the diagram to pull up more limited pathways, such as ceramide, neurotransmitter, ubiquinone, menaquinone, or fructan metabolism. Here is an example, depicting ketone body metabolism.

Clicking on and moving the vertical line between the menus and diagrams gives access to scrolling bars and more controls. Beyond human metabolism (KEGG’s “hsa” abbreviation), these databases also cover broad metabolic territory for other species, including primates, birds, and other animals, invertebrates, plants, fungi, one-celled organisms, bacteria (such as Firmicutes like Lactobacilli, or Actinobacteria like Bifidobacteria). In the KEGG Pathway Map view, clicking on the “hsa” button allows you to pull up only human metabolic pathways. On individual pathway diagrams, clicking on the “Reference Pathway” pull-down menu at the upper left allows you to see which organisms are known to utilize this pathway. For example, papaya, soybean, walnut, tomato, grape, and many other plants perform synthesis of flavonoids, while many bacterial and fungal species (among them many potential pathogens) are able to break down dioxins. While not directly applicable to human metabolism, these diagrams are nevertheless valuable for understanding how plants synthesize phytoneutrients and antioxidants of interest in the study of hormetics as well as how microbes deal with toxins. Also included are instructions for performing searches and lists of abbreviations used.

The broad range of information provided in KEGG makes it somewhat complex to use, but with a little practice, it can become a valuable tool for learning. Enjoy it in mental pleasure and physical health!
between providing effective yet affordable care while caring for enough patients to build a practice is often a greater challenge for independent doctors than most people appreciate. Restrictions in insurance payment limit the time a practitioner can spare for each patient, and not infrequently lead to burnout in practitioners and patients alike. More and more physicians are looking for alternative business models, and for many, monthly membership systems result in improved care and all-around satisfaction. We may come to discover that different schemes are better suited to 1) younger and/or healthier and 2) older and/or not-as-healthy patient populations—and that paying for wellness beats paying for illness. This recent JAMA article describes several burnt-out physicians’ searches for ways to provide authentic health care to people they can interact with in a humane manner that is meaningful for both.

Read more: https://jamanetwork.com/journals/jama/fullarticle/2680728

The Earth's Exposome Impacts Our Own

The exposome may be thought of as an incredible biological device that records everything you’ve ever encountered and what your response to it was each time, and it includes the epigenome—how your experiences alter the reading of your genetic code and its implementation in the elaboration of proteins in the body. But Earth itself has an exposome that is increasingly under siege from climate change, urbanization, pollution, greater human population, and loss of biodiversity, and this is reflected in a higher burden of asthma, allergy, and respiratory and gastrointestinal conditions. Because the immune system interprets and mediates the effects of outer influences, it is especially important to consider the paradoxical challenges posed to it by 1) increasing air, water, and soil toxin burden, 2) diets characterized by refined fats and carbohydrates, and 3) households ‘cleaned’ with microbicides and pesticides. This 2018 study explores the mechanisms behind how exposome interactions lead to hypersensitization, and it makes a strong case that preserving balance in the environment and in human lifestyles is a central means of easing the atopic burden.

Read more: https://www.jacionline.org/article/S0091-6749(18)30140-4/pdf