Nutrient of the Month: Cyanidin-3-Glucoside

Flavonoids are versatile phytonutrients, showing a broad range of beneficial metabolic effects. However, many are poorly absorbed, though those bound to sugars generally show better bioavailability. A gorgeous example of such a flavonoid derivative is cyanidin-3-glucoside (C3G), an anthocyanidin glycoside. Like other anthocyanins, this deep red-purple pigment is formed in plants in response to stress and aging/ripening, and has been found in a variety of dark-colored fruits and other food plants, including blue/purple corn, black beans, camu-camu fruit, bilberries, blueberries, purple cabbage, purple grapes, mulberries, black soybeans, hibiscus flowers, blackberries, carnation flowers, raspberries, black rice, olives, strawberries, pomegranate, purple eggplant, blackcurrants, gooseberries, barley grass, black elderberries, chokeberries, purple onions, and blood oranges. Also known as chrysanthemin, C3G shows **good bioavailability in humans**, and its metabolites include ferulic, hippuric, phenylpropanoid, and protocatechuic organic acids.

Like other flavonoids and anthocyanidins, C3G boasts numerous healthful properties, but C3G's catalog may be especially impressive by virtue of its bioavailability. The core from which these qualities radiate is strong defense against oxidative stressors and preservation of clean energy metabolism, actions that reduce cellular aging and are central to long-term vital organ function. It is interesting to note that among C3G's many following activities are several metabolic targets of drugs:

- **Reducing toxicity associated with acrylamide** and enhancing genetic expression of glutathione in human cells
- Protecting vascular and retinal functions through a variety of means detailed below
- Promoting apoptosis (programmed death) in "triple negative" breast cancer cells that lack estrogen, progesterone, and HER-2 growth factor receptor expression
and are thus particularly difficult to treat

- Limiting cognitive dysfunction caused by beta-amyloid, inhibiting tau protein activation, and improving related glucose signaling function in animals
- C3G's triple-ring structure gives it efficient reactive oxygen species scavenging, metal chelation, and radical quenching capacities; each anthocyanin molecule is estimated to quench ~125 oxygen radicals
- Positively impacting glucose, lipid, and insulin metabolism as described below
- Protecting brain neuron function in an animal model of cerebral stroke
- Inhibiting migration of strongly metastatic human lung cancer cells, partially by decreasing genetic expression of matrix metalloproteinase-2, an enzyme involved in tissue invasion and inflammation

In mice, C3G has been found to increase vascular nitric oxide production by activating endothelial nitric oxide synthase (eNOS) activity and heightening its genetic expression, and in human endothelial cells exposed to either the proinflammatory tumor necrosis factor-α or to palmitic acid (a saturated fat), C3G activated the master antioxidant enzyme regulator Nrf2 (nuclear factor erythroid-derived 2-like 2). These actions aid vascular tone and help limit oxidative stress, both of which are central in preserving healthy circulatory function. C3G also improved status of the major antioxidant glutathione in cytokine-challenged intestinal cells (through Nrf2 activation) as well as in glucose-challenged liver cells.

C3G also shows notable protective activity in the retina, increasingly valuable in those using computers and electronic devices. In human retinal cells exposed to damaging light levels, C3G inhibited aging-related changes in glucose metabolism as well as genetic expression associated with deleterious formation of new blood vessels. In light-exposed animals, C3G reduced retinal cell death and retinal angiogenesis by boosting production and expression of Nrf2 and the antioxidant enzyme hemeoxygenase. Laboratory experiments also demonstrate that C3G limits age-related photooxidative processes and protects the retinal photoreceptor rhodopsin, which is associated with better night vision.

In mice with diabetes or diet-induced obesity, C3G improved insulin sensitivity and decreased fasting glucose levels and fatty liver accumulation while reducing markers of adipose tissue inflammation. In another mouse study, it was found to induce muscle glucose transport signaling related to AMPK (adenosine monophosphate kinase), a top-level cellular energy regulator. In fat cells, C3G elevated activity of PPARγ (peroxisome proliferator-activated receptor-gamma, a transcription factor in the regulation of carbohydrate and lipid metabolism), aiding glucose transport in a manner consistent with reduced insulin resistance. In a well-designed laboratory study, C3G caused fat cells to mature into smaller cells having greater PPARγ gene expression, and in muscle myotubes it improved expression of PGC1α and Sirt1 (PPARγ coactivator α and sirtuin 1, factors deeply involved in cellular aging, energy regulation, and mitochondrial formation). The incidence of diabetes (including gestational diabetes) has been increasing rapidly worldwide, and the metabolic mechanisms by which C3G and other food polyphenolics function have been noted as potentially beneficial in its prevention and treatment.

Baking (and perhaps other forms of heat processing) can greatly decrease food C3G contents, and thus consuming fresh or minimally processed food sources is recommendable. The transformation of C3G begins in the mouth, but the human microbiota appears to be an important component in its bioactivation. C3G ends up in organs and tissues throughout the body, including the adipose, and there are also urinary and breath metabolites. Americans apparently have relatively low intakes of anthocyanins compared to Koreans and Europeans.

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**2018 Thought Leaders Consortium: Chronological Age vs Biological Age**

Our understanding of the science of aging is evolving as a result of new discoveries, enhanced technology, and collaborative research. We now know chronological age (birthdays) is not an equal measure of biological age (function). This future-forward
The concept is going to impact health care on so many levels. Explore it with PLMI and our expert faculty at the Sixth Annual Thought Leaders Consortium in Tucson this fall. Attendees from more than 12 countries have already registered and seats are filling fast.

Video Link: https://vimeo.com/277329664

The Sixth Annual Thought Leaders Consortium
The Science of Precision: What’s Next for Personalized Lifestyle Health Care
October 12-13, 2018
The Westin La Paloma Resort & Spa
Tucson, Arizona

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Resource Spotlight: BBC Libraries on All Things Microbiome

It’s just been seeded by BBC, but it’s growing rapidly and is beginning to cover the body’s microbiomes and the associated genomes that so outsize our own, as well as how both of these entities affect and reflect our health. Second Genome is the story of BBC’s journey down the rabbit hole of the gut and beyond.

- In this weekly series of 30-minute segments, correspondent James Gallagher interviews leading scientists, examines the research, and begins to understand that we all carry a formidable alien organ whose friendliness towards us is predicated upon what we eat and how we live.
- This collection of brief clips highlights new findings and noteworthy insights from the experts.
- Related audio and video presentations explore a tribal society’s microbiome, Robogut, fecal transplant therapy, and The Age of the Genome.

If this informative website is any measure, knowing your ratio of Firmicutes to Bacteroidetes and whether or not you harbor Akkermansia is on its way to becoming a social measure of commonality and individuality, and we can look forward to upcoming installments on how the microbiome impacts mental health. Though interpretations of microbiome composition still vary a great deal, BBC is doing a great job of conveying the importance of this complex topic while also giving listeners a good laugh.

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

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