October 2019 - Mid-Month Bonus Newsletter

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Nutrient of the Month: Melatonin

If vitamin D is the sunshine vitamin, then melatonin might be thought of as the moon-phase nutrient, as its secretion by the body is dependent upon how much continuous, complete, and uninterrupted dark you receive during your sleep period. Having a distinct day-versus-night variation in melatonin secretion is even thought by some to be one determinant of successful aging. This pineal hormone is the final product of conversion of tryptophan to 5-hydroxytryptophan to serotonin to acetylserotonin, culminating in a very active indoleamine: N-acetyl-5-methoxytryptamine, AKA melatonin. Considerable amounts are synthesized in the intestines, where it influences gut motility, and can also be made by the skin, bone marrow, thymus, mitochondria, salivary glands, immune cells, and in other tissues, where it may help control the redox environment. It is also found in breast milk.

Early in evolution, melatonin may have originated in bacteria, and levels in mitochondria (which may, incidentally, have started as bacteria), are particularly high; it found in many plants, including feverfew leaf, skullcap herb, algae, cherries, ginger, corn, onion, barley, walnut, oat, pomegranate, and apple. Some may think of melatonin as merely a dietary supplement, but it is a true hormone involved in high-level, long-term regulation of higher functions like sexual maturation, epigenetic events, seasonal immune balance, chronobiology of other hormones, and some cellular aging processes. For this reason, it is recommendable to be aware of common lifestyle impacts on the body’s production of melatonin:

- Most important: receiving sufficient (but not excessive) light followed by sufficient dark is paramount for normal secretion; light inhibits while dark induces pineal secretion, in a strategic daily rhythm
- Exposure to artificial light at night (particularly blue light) may especially disrupt
Caffeine may lower natural secretion

Meditating at night may increase circulating levels

Well known for helping adjust sleep/wake rhythms and improving sleep efficiency in children as well as adults, melatonin can temporarily lower alertness, body temperature, and blood pressure after supplementation. A common theme in preclinical studies on melatonin is its prominence in coordinating healing, managing the stress response after injury, and transitioning through the phases of the life cycle—all of which, after all, may best be cultivated during sleep.

Melatonin works in the watery milieu within cells as well as their fatty membranes, and it easily enters cell nuclei and mitochondria and passes through the placental and blood-brain barriers. As one of the body's more powerful and ubiquitous antioxidants, it has considerable capacity to improve cells' redox status and thereby influence whether they are able to perform autophagy (cellular 'housekeeping' and recycling of damaged structures, deeply affected by lifestyle) to optimize cellular function or whether they must resort to cellular sacrifice in apoptosis. Melatonin also helps regulate gene expression of sirtuins and other factors in the cell life/death signaling network that help mediate the progress of health and disease over time. Interestingly, this crucial antioxidant may act differentially in cancer cells' mitochondria to encourage apoptosis, and reduced pineal melatonin production with biological aging may partially explain the heightened risk for cancer with age.

A few other interesting findings regarding melatonin:
- It is a factor influencing stem cell proliferation, migration, differentiation, and reprogramming
- It is involved in energy metabolism at multiple levels (e.g., insulin sensitivity, brown fat activation); eating habits and modern lighting can block these and encourage obesity
- In wide-ranging preclinical research, it has shown numerous epigenetic, immune, and redox-related effects on cancer mechanisms
- Preliminary research suggests that it may help preserve telomere length during aging, though broader study is needed
- It appears to modulate pain perception in humans
- In healthy young men, it enhanced an aspect of functional memory under stressful conditions, apparently separate from effects on the stress response
- It may help control autophagy in the central nervous system in injury, toxin exposure, or aging, and early research suggests it could, in some circumstances, upregulate brain-derived neurotrophic factor (BDNF)
- Endogenous or supplemental melatonin may modulate the oral inflammatory response
- In healthy men it advanced heart rate variability timing and in aged men it had an early-hour hypotensive effect; these may indicate benefit against morning heart events, though confirmation is needed
- It may affect liver enzyme test results
- Some melatonin receptor gene variants appear to increase risk for diabetes
- In the microbiomes of obese mice, it increased gut abundance of metabolically desirable Akkermansia and reduced the ratio between Firmicutes and Bacteroidetes phylum members
- Hair follicles and skin cells express receptors for melatonin

As melatonin may interact with or alter metabolism of many common medications (even in paradoxical ways, as in the case of blood pressure drugs) and change levels of other hormones in the body, it is recommendable to consult with a knowledgeable health care practitioner before taking this highly active hormone.
Response to toxins and stressors can help either build health or wear it down. This news story provides a summary of recent research findings into numerous genomic and microbiome testing procedures and how they help guide the path to wellness—on a personalized basis.

News story:

https://www.naturalproductsinsider.com/ideation/personalized-nutrition-translating-research-solutions

Resource: A Specialized Resource for a Flourishing Phytonutrient Class

Food polyphenols are pretty special. Whether considering the better-known members like quercetin, resveratrol and curcumin or learning about newer up-and-comers like pterostilbene, carnosol, tyrosols, and ursolic acid, we have really just begun to understand their roles in human, animal, and planetary health:

- They are crucial for plant protection and survival in the face of increasingly difficult growing conditions
- They are critically important signaling molecules and antioxidants within foods as well as within people or animals consuming them
- Increasing numbers of them are being studied for how they modulate immunometabolic, cognitive, cardiovascular, digestive, detoxification, and other functions
- Some are showing up as surprisingly effective prebiotics for supporting beneficial gut microbes

As a class (molecular, phytochemical, or otherwise) polyphenols represent a gargantuan population, and research findings on this dynamic group of compounds (not to mention their metabolites) is increasingly significant to -omics studies as well as to nutrition. **Phenol Explorer** is a handy European database focusing on food contents of polyphenolics, and it provides information on around 500 of these substances as found in hundreds of foods. While “flavonoid” may be the most widely recognized term for polyphenolic substances, it is vague and comprises numerous subclasses of polyphenols while excluding others. **Specific subtypes of polyphenols** included in this database include anthocyanins, chalcones and dihydrochalcones, flavanols, flavanones, flavones, flavonols (including catechins and procyanidins) and dihydroflavonols, isoflavonoids, lignans, phenolic acids, stilbenes, coumarins, and other related compounds. Pull-down menus link to individual polyphenols such as xanthohumol, cyanidins, epicatechin, and resveratrol, provided you click on the “Details” button rather than clicking on the name of the polyphenol itself (which can be briefly confusing). The main page for each polyphenol then provides links to food contents, metabolites, and other available features.

The fascinating field of polyphenolics is growing rapidly, and names—proper, chemical, molecular, improper, and outright mistaken—abound. If you’re not certain of the class or chemical name of a particular polyphenol, you can simply type a term into the general search field located at the upper right corner of virtually every page in this website. As an example, while searching for “rutin” pulls up 22 related terms, though it fails to clarify that “quercetin 3-O-rutinoside” is a valid synonym for the term “rutin” while most of the other 21 simply contain the letter sequence “-rutin-” somewhere within their names. One work-around for this confusion (which is only sure to increase as more polyphenols are discovered, more deeply studied, characterized, and re-characterized) is to use
PubMed’s trusty MeSH (Medical Subject Headings) search to identify precise synonyms for such potentially equivocal search terms; MeSH correctly points out (middle of page) that ‘quercetin-3-rutinoside’ is a proper synonym for rutin.

Food contents can be searched by classes of foods, including numerous vegetables, fruits, grains, legumes, oils, beverages, and herbs/spices. As one example, searching with the word “tomato” in the general search field (again, in the upper right corner) pulls up tomato juice, raw, paste, ketchup, cherry tomatoes, and yellow tomatoes. Because food varieties and handling techniques (peeling, cooking, storage, etc.) can substantially influence polyphenol contents, Phenol Explorer includes a section devoted to salient research findings organized into reports on particular food types; for example, this one detailing the many varieties of olives from European regions and California, differences between black and green olives, differences between olives and olive oils, and changes induced by maturation, fermentation, and stress. (Who knew that black olives are black because of anthocyanins?)

Another of the database’s distinctive offerings is a feature called “Retention Factors,” (included in each polyphenol’s main data page under the “mean RF value”) which is a decimal fraction reflecting the proportion of original contents of that polyphenol that remain after processing. In the example of cyanidin-3-glucoside (described in the July 2018 bonus issue of PLMI’s Health is Personal newsletter), different research articles have found that freezing red raspberries may reduce their C3G contents by about half compared to their raw form, with a link provided to a citation for the related study.

Phenol Explorer additionally captures detail regarding polyphenols’ metabolites in humans and animals as described in scientific literature, complete with links to citations. Here, for example, is the summary page of study results provided for equol, the desirable human metabolite of soy isoflavones; a nice feature is the inclusion of graphics (under the “Kinetic data” column) demonstrating the timing and plasma levels of metabolites as they appear and are removed from circulation.

This database also provides a helpful FAQ section explaining how data has been gathered, evaluated, and expressed in Phenol Explorer, and for molecular experts, it even provides a clever drawing tool for depicting (or importing, or searching for by molecular weight) chemical structures for searching or comparing against others—complete with YouTube usage tutorial.

Why are black olives black? Anthocyanins!
The Phenol-Explorer Database is full of useful tools and interesting information.
Newsletter Team
Jeffrey Bland, PhD - Publisher
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Trish Eury - Content Editor
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