December 2018 - Mid-Month Bonus Newsletter

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Nutrient of the Month: Folate/Folic Acid

Folate has recently been called a "Jekyll and Hyde" nutrient, as either insufficiency or excess of it can allow cancer-related mechanisms to take place. Food sources of folate are generally in formyltetrahydrofolate form and the active form of folate in the body is methyltetrahydrofolate, which has been ‘readied’ for human metabolism by being chemically reduced and methylated through multiple reactions. Folic acid, which is generally shelf-stable (though ultraviolet light can degrade it), is not a naturally-occurring form of folate, yet “folic acid” may be more familiar because this form of folate has been used in fortification of foods like bread, rice, cereal, pasta, and crackers for decades. However, folic acid has not undergone the reactions necessary to prepare it for participation in body chemistry. The best food sources of folates are leafy green vegetables, and food-based folates can also be destroyed by ultraviolet light as well as exposure to acids or high heat.

It’s long been understood that receiving enough folate is especially important during pregnancy, and in earlier times when folate deficiency was more widespread, supplementation and food fortification with folic acid proved to be a successful, low-cost means of reducing birth defects. However, folate serves many functions in the body, including:

- preserving the integrity of DNA
- triggering genetic activity and influencing epigenetic patterning
- aiding maturation processes in stem cells
- building and repairing tissues (fetal and adult)
- creating red and white blood cells
- facilitating nucleotide (and thus DNA/RNA), neurotransmitter, and amino acid synthesis
- helping recycle homocysteine, a metabolite that in excess can be a cardiovascular and neurological toxin
Folate cooperates extensively with other B-family vitamins (especially B12 and B6, but others as well), betaine, choline, iron, and antioxidants in these many roles. Folic acid unquestionably helps prevent mutagenesis and birth defects, but can an excess of folic acid "feed" an existing cancer? In this Food for Thought video, Dr. Jeffrey Bland discusses the many hats worn by folic acid, the controversies surrounding folic acid fortification, and its interactions with other metabolic players.

Because folate plays so many crucial roles in the body, it is metabolized by multiple enzymes, each of which are subject to genetic variations in functionality. There is a manifold difference among people in capacity for activating folic acid, yet humans are relatively inefficient at this compared to other mammals. The body’s utilization of synthetic folic acid depends upon having enough of the enzymes needed for activation, and insufficiency or imbalance among these enzymes can cause unmetabolized folic acid to build up in circulation. High levels of unmetabolized folic acid can negatively affect the activity of enzymes needed for its metabolism and has been linked to anemia, colon cancer, altered immune function, and lower cognitive test scores.

There is some concern that excess circulating unmetabolized folic acid could even be oxidized into a genotoxic substance. High folate levels can force vitamin B12 deficiency or precipitate epileptic seizures in susceptible persons, reinforcing the idea that co-fortifying with both of these closely-linked nutrients may often be recommendable. Insufficient levels of folate or excessive levels of unmetabolized folic acid or folate could also increase risk for autistic spectrum disorders. Food fortification programs have been successful at reducing the incidence of folate deficiency, yet those consuming more fortified products may carry higher levels of unmetabolized folic acid.

High-dose supplementation with either folate or folic acid could potentially have detrimental effects on cellular methylation patterns, yet insufficiency can affect genomic integrity and lead to mutagenic changes, and yet again, excessive intake may also encourage the growth of established cancer cells. Clearly, either too little or too much of this necessary but seemingly picky vitamin can have serious consequences, so where is "The Folate Zone"? What is a good daily dosage of folate? The answer is different for each individual, and depends not only on genetic variants in folate enzymes (not to mention folate receptors and blood-brain barrier variables) but also on personal and family medical history, reproductive status, lifestyle factors, and intakes of other nutrients (like those mentioned above) whose missions are closely tied to folate. However, in the absence of individualized genetic evaluation, a basic recommendation that most researchers would seem to stand behind would be to limit total daily folate intake to no more than about 800-1000 micrograms daily yet constrain intake of synthetic folic acid to no more than 400 micrograms as part of this total daily folate intake. An important consideration is to take folate along with its nutritional partners, whether in a multivitamin supplement or separately, in order to optimize the necessary cooperative balance among them. Drugs that can interfere with folate metabolism include valproic acid, sulfonamides, trimethoprim, and methotrexate.

Folate represents just one example among many in which selectively increased consumption of a single nutrient, divorced from its “team,” may lead to unintended consequences. Much as with antioxidants or amino acids, essential nutrients work together, and imbalance among team members can destabilize carefully established metabolic equilibrium. Though “picky” about its dosage level, folate epitomizes the interactive character of nutrition, working closely with related nutrients and feeding the body’s information-gathering systems in four dimensions to help adapt metabolic function in future as well as present generations.

Resource: Making Sense of Scents—Functions of Aromas Beyond Smell

In humans, plants, and animals, aroma compounds can variously aid identification, communication, and defense, in addition to signaling...
ripeness of food plants and contributing to their flavor. According to the developers of the recently-inaugurated aroma database *AromaDb*, there are around 300 active olfactory receptor genes involved in detecting and triggering responses to aroma molecules, such as modulation of brain function, cell signaling, and other aspects of physiology. The AromaDb integrates information on aromatics’ sources, chemical types, structures, properties, and bioactivities, and is described in this August 2018 article in Frontiers in Plant Science.

The AromaDb *Plant search page* allows searching by Latin name for select plants, and search detail entered immediately brings up all iterations from both genus and species fields; for example, entering "rosa" brings up common name Palmarosa and species name *tuberosa* as well as genus name *Rosa*. Clicking upon the plant’s essential oil field brings up listed constituents; as an example, *Abies alba* (silver fir) essential oil is listed as consisting of alpha-pinene (19.8%) and limonene (11%) in addition to dozens of other aromatics. The *Aroma Molecules page* discloses further detail about the chemical class and fragrance type of particular odor molecules; for example, *beta-caryophyllene* (recently discovered to have endocannabinoid potential) is revealed as a sesquiterpene compound with a spice-class fragrance.

Because the same plant species can be provoked to develop a different aroma profile under different growing circumstances, the AromaDb also includes information on these different plant “chemotypes.” The *Essential Oil search page* allows searching by plant Latin name for known aroma compounds, and provides known breakdown by percentage; for example, this analysis of rosemary reveals its major camphor and cineole chemotypes and details other listed aromatics. Clicking upon individual aroma constituents accesses further detail; for example, *beta-ionone* and *beta-damascenone*, important contributors to floral scents, are shown in 2D and 3D structures and are both predicted by Ames testing to be non-mutagenic.

Not yet fully populated, this resource based in India (the cradle for many aromatic materials and compounded perfumes) continues to integrate data on non-Indian plants and shows promise in aiding understanding of the many roles played by aromas.

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**Interaction to Boost Individual Function**

Since the Latin root of the word doctor actually means teacher, does it follow that learning is a kind of medicine? Epigenomic science has established that subjective and objective perceptions can alter the way genes are regulated, and because many health imbalances arise as the result of disharmony between desired functional outputs and lifestyle, social, and environmental inputs, changing thinking and behavior patterns can often effect considerable improvement.

An innovative British health initiative is looking into ways interactive and creative activities can help treat, mitigate, and prevent disease. Termed “social prescribing,” it aims to enhance health by incorporating arts, sports, hobbies, and social outings into lifestyles that may otherwise lack such outlets; it could also be thought of as a kind of medicinal continuing education to help health-challenged individuals maintain or even build their at-risk capabilities. These therapeutic social engagements can improve mental and physical outputs such as communication, confidence, and concentration in those diagnosed or at risk for certain conditions; for instance, singing to aid verbal skills or visiting museums to inspire and buoy the moods of lonely participants. Improving practical skills may also accrue health in other ways; for example, making craft items can build muscle strength and coordination, and learning new methods of cooking can broaden nutritional foundations. “Prescribing” these kinds of activities will, of course, depend on local offerings and capacities, but programs are already underway in several
regions of England, Wales, and Canada, and their outcomes will clarify budgetary impacts and long-term sustainability.