SUPPLEMENTING THE HEALTH-SPAN: BENEFICIAL ANTI-AGING NUTRACEUTICALS, REGULATED BY FDA AND FTC

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Extending the Health-Span, at Sky Song
Introduction and Overview

- Dietary Supplements, a food category created by Congress in 1994 with DSHEA
- Not about Safety, but about anti-aging claims supported by science, herbal & dietary ingredients (and foods) with therapeutic value for chronic diseases—re benefits and efficacy.
- Overview of how FDA and FTC both regulate supplements
- Major herbs with anti-aging benefits: Resveratrol, Bilberry, Turmeric, Astaxanthin
- Several other nutrients and herbs that extend the Health-span
- Super foods & lifestyles that extend the Health-span
- FTC enforcement vs. unsupported memory claims
- The promise of Medical Foods for the future?
FDA Regulation of Supplements

- No FDA preapproval required, because supplements are not drugs, in the food category; may not make drug or disease claims.
- Per Sec. 6 of DSHEA, structure/function (s/f) claims allowed
- But must have Substantiation, defined by FTC as:
  For valid structure/function (s/f) claims, the FTC demands a high level of documentation and support for supplement claims: “competent and reliable scientific evidence.” The Commission’s standard is further defined and detailed in many Consent Decrees and court orders as: “‘Competent and reliable scientific evidence’ shall mean tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.”
- Per 21 CFR sec. 101.93 (g), disease is defined:
  (g) Disease claims. (1) For purposes of 21 U.S.C. 343(r)(6), a “disease” is damage to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g., hypertension); except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition.
Structure/function Claims

§6. Statements of Nutritional Support. [= structure/function claims]

Section 403(r) (21 U.S.C. 343(r)) is amended by adding at the end the following:

"(6) For purposes of paragraph (r)(1)(B), a statement for a dietary supplement may be made if -

"(A) [4 types] the statement claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, [e.g., vitamin C for scurvy]; describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans, characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or describes general well-being from consumption of a nutrient or dietary ingredient,

"(B) the manufacturer of the dietary supplement has substantiation that such statement is truthful and not misleading, and

"(C) the statement contains, prominently displayed and in boldface type, the following: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." [the Disclaimer on supplement labels]
FTC Regulation of Supplements

• Test: What is the ad’s “overall net impression” to the average consumer
• All material claims—express and implied—that consumer relies on for purchasing decision (vs. sales puffery)
• All claims must be true, accurate, not misleading, and have adequate Substantiation
• Are consumers, esp Seniors, being defrauded of $$$
• Testimonials & Endorsements—are imputed to the Marketer; requirement of Disclaimers to “cure” deception
• Operation Cure.all: Focus on bogus claims for weight loss, and anti-aging
• Recent cases: POM Wonderful “risk of cancer” (deferred to the FDA: no authorized health claim re pomegranates)
FDA & FTC—joint oversight & regulation

• Both are consumer protection agencies—health, wellness, beauty (not Rx drugs, devices)

• FDA & FTC have joint jurisdiction, MOU of 1983

• Joint actions vs. swine & avian flu “supplements” and 9/11 remedies, e.g., “Herbal Cipro”

• FTC demands that health claims (e.g., Calcium may reduce your risk of osteoporosis) be FDA-authorized first

• Websites are considered both “labeling” & marketing

• Both agencies look at social media, e.g., FDA Warning Letters re Facebook “likes”

• State Actions: AG’s, False advertising, Unfair Business Practices
S/f Claims re Aging Permitted by FDA (2000)

- Hot flashes, and other common symptoms associated with the menstrual cycle
- Morning sickness associated with pregnancy
- Mild mood changes, cramps, and edema associated with the menstrual cycle
- Mild memory problems associated with aging
- Hair loss associated with aging
- Improves absentmindedness
- Wrinkles
- Liver spots and spider veins
Benefits of Resveratrol

• Resveratrol is a naturally occurring compound found in grapes, red wine, berries, chocolate, and peanuts.

• Resveratrol has been linked to activating sirtuins, a type of protein involved in aging biology as well as other cellular pathways. As of 2010, was thought to be a miracle botanical—drug studies as well.

• Recent studies report Resveratrol’s ability to extend the life span of some model organisms and protect against age-related diseases in animal models, including neurodegeneration in rodent models with Alzheimer’s disease.

Recent Resveratrol Studies—pro & con

• Currently it is unclear whether resveratrol has any effect on human health or aging, but current clinical trials have provided evidence that resveratrol impacts neuroinflammation when given to patients with mild or moderate Alzheimer's disease.

• One recent study demonstrated what researchers consider conclusive evidence that resveratrol directly activates a protein that promotes longevity in animal models.

• Conversely other scientific studies indicate no association with lifespan, heart disease or cancer protection. Thus, the science is equivocal.

• In a phase 2 clinical study, participants received resveratrol orally or a placebo over a 52-week period. Resveratrol was detected in both CSF and plasma.

Benefits of Bilberry

- Bilberry has a high concentration of antioxidants called antocyanins. It is reported to have anti-inflammatory and lipid-lowering effects, and to promote antioxidant defense and lower oxidative stress.

- These effects and defenses are valuable in the treatment or prevention of conditions associated with inflammation, dyslipidemia, hyperglycemia or increased oxidative stress, infection, burns, cardiovascular disease, cancer, diabetes, and dementia and other age-related diseases.

Benefits of Turmeric

- Turmeric has been known to provide benefits to disorders which are associated with aging.
- Turmeric is used as a dietary supplement for arthritis, stomach, skin, liver, and gallbladder problems, cancer, and other conditions.
- Turmeric may ward off heart attacks, delay diabetes, fight cancer, protect the brain, and curb joint pain.
- A trio of studies show that naturally-occurring chemicals in turmeric root appear to protect the heart from aging, in a manner similar to moderate aerobic exercise.
- Studies also site turmeric’s anti-inflammatory and antioxidant properties.

Recent Turmeric Studies—Anti-inflammation

• Other “bridge” studies show that chronic inflammation is linked to many chronic and age-related diseases, e.g., cancer, stroke, & Alzheimer’s.
• An opinion article in The Observer in 2015 was entitled “Inflammation: The Battle to the Death Inside Our Bodies”
• Often, chronic disease development stems from an unresolved inflammatory response.
• A coalition of experts published a consensus in 2015 in the British Journal of Nutrition that nutrition influences inflammatory processes and can help reduce the risk of chronic diseases.
• Some scientists believe that 70% of all diseases are due to inflammation.

Benefits of Astaxanthin

- Astaxanthin is a member of the carotenoid family and is found mainly in algae and aquatic animals. It is well known for its antioxidant capacity.
- Numerous studies have linked Astaxanthin to potential health-promoting effects in the prevention and treatment of diseases, such as cancers, chronic inflammatory diseases, metabolic syndrome, diabetes, cardiovascular diseases, neurodegenerative diseases, gastrointestinal diseases, liver diseases, neurodegenerative diseases, eye diseases, skin diseases, exercise-induced fatigue, male infertility, and renal failure.
- Some studies suggested increased consumption of anthocanins is associated with lower risk of cardiovascular disease and hypertension and increased consumption of anthocyanin-rich fruit is associated with a lower risk of development of type 2 diabetes.

Recent Astaxanthin Studies

- A recent double-blind study of 39 subjects reporting awareness of fatigue were divided into two groups, one that received astaxanthin and tocotrienols, the other received tocotrienols. Subjects found that astaxanthin significantly reduced perceived symptoms of mental and physical fatigue, including improvements in clarity of thinking, concentration, motivation, and mood.

- Astaxanthin may improve cognitive functions. In an open label study, ten men, ages 50-69, received astaxanthin for 12 weeks. Using a computerized test designed to detect cognitive deterioration, the men showed improvements in reaction time, attention, and working memory.

Other Supplements for Healthy Aging

- Red Yeast Rice— a Chinese food/ herb vs. high LDL
- Fish Oil, Omega-3’s— anti-inflammatory, vs heart disease
- CoQ10— healthier aging; Dr. Andrew Weil suggestions 100 mg/ day
- Lutein & Zeaxanthin— vs. night blindness & macular degeneration
- Pomegranate (juice & extract)— antioxidants, some evidence vs. cancer
- “Superfruits” sold as supplements: Acai, Mangosteen, Noni, Goji berries, Sea Buckthorn (orange, also used in cosmetic topicals): strong antioxidants
- Adaptogenic herbs vs stress: Aswagandha, Holy Basil, Lemon Balm
- Collagen & BioSil— bones, hair, nails, skin
- Vitamin D3 — vital for immune system
- Vitamin B complex— heart disease & Alzheimer’s
- Wild oregano oil (Oreganol P-73)— immune system
- Ginkgo biloba— better memory in older age
- Vitamin C & E may protect vs Alzheimer’s & brain decline: a 2017 study, data from over 5,200 seniors, fewer AD
FDA-authorized Health Claims

Health Claims are claims linking a food or substance to a reduced risk of disease. These claims must be pre-authorized by the FDA, after showing “significant scientific agreement.” Can take up to 5 years of FDA review.

§ 101.72 calcium, Vit D and osteoporosis
§ 101.73 dietary lipids and cancer
§ 101.74 sodium and hypertension
§ 101.75 dietary saturated fat and cholesterol and risk of coronary heart disease (“CHD”)
§ 101.76 fiber-containing grain products, fruits, and vegetables and cancer
§ 101.77 fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of CHD
FDA Health Claims—some Qualified

Note: not disease prevention claims; not drug claims

§ 101.78 fruits and vegetables and cancer
§ 101.79 folic acid and neural tube defects
§ 101.80 dietary noncariogenic carbohydrate sweeteners [sugar alcohols], including sucralose, and dental caries
§ 101.81 soluble fiber from certain foods [oat bran and whole oats, barley] and risk of CHD
§ 101.82 soy protein and risk of CHD
§ 101.83 plant sterol/stanol esters and risk of CHD

More recent health claims from FDA are qualified, very muted; thus, not good marketing. (See over)
Health Claims --Qualified

No significant scientific agreement; limited science, and many qualifiers:

“**Selenium** may reduce the risk of certain cancers. Some scientific evidence suggests that consumption of selenium may reduce the risk of certain forms of cancer. However, FDA has determined that this evidence is limited and not conclusive.”

“Some scientific evidence suggests that consumption of **antioxidant vitamins** may reduce the risk of certain forms of cancer. However, FDA does not endorse this claim because this evidence is limited and not conclusive.”

“Very limited and preliminary scientific research suggests that eating one-half to one cup of **tomatoes and/or tomato sauce** a week may reduce the risk of prostate cancer. FDA concludes that there is little scientific evidence supporting this claim.”

“One study suggests that consumption of tomato sauce two times per week may reduce the risk of ovarian cancer; while this same study shows that consumption of **tomatoes or tomato juice** had no effect on ovarian cancer risk. FDA concludes that it is highly uncertain that tomato sauce reduces the risk of ovarian cancer.”
Super Foods for Healthy Aging

- Mediterranean diet—Olive oil, little red meat, lots of fish, beans & greens, grains, Pasta!, nuts, wine, few sweets
- Honey and agave syrup—vs sugars & artificial sweeteners
- Eggs: moderate consumption may boost brain functions (2017); a Meta-analysis shows eggs can reduce stroke risk by 12%
- Rainbow of vegetables, esp cruciferous veggies vs cancer
- Sulfuraphane in young broccoli sprouts—anti-carcinogen?
- Yogurt & Kefir, probiotics—1/2 of immune system is in the gut
- Coffee, green tea—reduced risk of dementia
- Brown rice, quinoa, older grains
- Fatty fish—salmon, tuna, sardines
- Kale, spirulina, dark chocolate
- Flax seed oil—anti-inflammatory
- Lots of fruits—esp berries for the Brain

Sources: Available upon request.
Senators ask FTC to Examine Memory Claims

- Sen. Claire McCaskill became concerned about supplement products targeted at seniors that claimed they improved age-related mental decline such as memory, and treated dementia and Alzheimer’s.

- McCaskill argued for increased regulation and the implementation of a systematic approach to prevent mislabeled and fraudulent products from entering the market. Specifically, she asked the FDA and FTC to focus on supplements containing highly processed or synthesized ingredients that do not occur in nature.

- In response to her complaints, the FTC brought charges and settled with one dietary supplement, Procera, for $1.4 million for unsubstantiated claims that it made in its advertisements about the effects of its supplement on age-related memory conditions.

FTC vs Claims for Lumosity

- Lumosity is a computer program that consumers use to train core cognitive abilities through games.
- In 2016, the FTC settled claims with the creators and marketers of Lumosity who agreed to pay $2 million in redress and notified subscribers on how to cancel their subscription.
- The FTC alleged that Lumosity deceived consumers with unfounded claims that the games helped users perform better at work and in school, and reduced or delayed cognitive impairments associated with age and other serious health conditions.
- “Lumosity preyed on consumers’ fears about age-related cognitive decline, suggesting their games could stave off memory loss, dementia, and even Alzheimer’s disease, but Lumosity simply did not have the science to back up its ads.” Jessica Rich, Director of the FTC’s Bureau of Consumer Protection

Calorie Restriction & The “Fast” Diet

• Since 1930s known lower food intake =longevity in rodents.
• Test this in rhesus monkeys (genetically 93% identical to humans), w same aging process and same diseases
• In 1980s, a controlled experiment with these monkeys, w diet cutting calories 30% from the regular, control diet
• By 2016, the control monkeys were chubby had 2.5 times the risk of age-related disease: cancer, diabetes, & heart disease
• A small German study reported that older people who cut calories for 3 months did better on memory tests—promising.
• The 5:2 Fast Diet: women had better insulin function, thus lower risk for diabetes, heart disease, cancers & possibly even dementia. Better results than cutting 25% of calories.

Sources: Available upon request.
Lifestyle Interventions: Holistic

• **The Okinawa Program**: On this Island of Japan, more centenarians than in any other place, due to diet (sweet potatoes, fish, wheat noodles), farming, relaxed view of time, can-do attitude, social kindnesses, close extended families.

• **Seventh Day Adventists**: vegetarians, religious & social networks. Live 7 years longer than other Americans.

• One of the Blue Zones of longevity in the world.

• **The Greek Island of Ikaria**: organic farms, beans & greens, herbal teas, home-made yogurt, meat (pork) only a few months per year, 2-3 glasses of wine per day, social interaction, dancing, lots of sex all through the 80s—dying of old-age. And an interesting picture at the end of the article.
Medical Foods—anti-aging for Future?


21 U.S.C. sec. 360ee(b)(3) The term "medical food" means a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

• Mid-way between Supplements and Rx Drugs –legally and medically
• **No FDA pre-market approval required**, but ingredients must be GRAS
• But closer to drug studies required, human clinical trials
• Food-based GRAS ingredients: fewer side effects & safer than new drugs
• Delivery may be in liquids, shakes or enteral—not necessarily via pills

Chronic diseases of aging are amenable to MFs: Limbrel & [dietary management of] OA, Fosteum & osteoporosis, Foltx & hyperhomocysteinemia, MYO & sarcopenia (astaxanthin, zinc, Vit D), Axona & symptoms of mild to moderate Alzheimer's, using MCTs
Questions?

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