

SIGN OF THE TIMES

Common Supplements for the Practicing Internist

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Practicing internists today frequently encounter patients who are interested in taking natural supplements. The usefulness and the potential complications of different compounds are sometimes difficult to tease out from the abundant (and often confusing or erroneous) information available to patients and clinicians. However, there are a few common ailments for which supplements are commonly used and may, in fact, be beneficial. Prominent among these therapies are turmeric and fish oil.

Turmeric, a familiar component of Indian cuisine, has a long history of use as a potent anti-inflammatory agent. Because anti-inflammatory medications have a multitude of complications, many patients seek out natural anti-inflammatories. Recent research demonstrates that the active compounds in turmeric, called curcuminoids, inhibit pro-inflammatory transcriptional activators—the “on-off” switches responsible for transcribing inflammatory cytokines and interleukins.

To ensure that a patient takes adequate concentrations of curcuminoids, standardized products should be used. Typical doses are 1500 mg taken up to three times daily. When turmeric is combined with piperine, an extract of black pepper, systemic absorption is significantly increased. Ingesting turmeric without pepper allows for localized gastrointestinal anti-inflammatory activity, which can be useful in inflammatory bowel disease (IBD). The clinical effect of turmeric in IBD is currently under study.

Fish oil had been used as a supplement for many years to lower triglycerides and is now endorsed for this purpose by the American Heart Association and the FDA. Although treatment of hypertriglyceridemia is the

accepted indication for fish oil, the canonical omega-3 component, which is readily incorporated into leukocyte cell membranes, also functions as an anti-inflammatory agent. Regular ingestion of fish oil decreases the ratio of omega-6 to omega-3 fatty acids in the cell membranes, thus reducing the amount of omega-6 substrate available for the production of arachidonic acid-derived inflammatory metabolites. Improvement in IBD symptoms in patients taking fish oil has been chronicled.

The main long-chain fatty acids in fish oil are EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid). Typical anti-inflammatory dosing is based on the EPA concentration and ranges from 500 to 1500 mg of EPA daily. Caution should be exercised in patients using concomitant prescription anti-coagulant therapy.

Red yeast rice (RYR) is a very popular alternative to statin drugs. It is a fermented rice product that gets its distinctive color from the mold species *Monascus purpureus*. Lovastatin was actually first isolated from red yeast rice in the early 1970s. In fact, red yeast rice actually contains several compounds with HMG-CoA reductase activity. When originally sold, the supplement was very popular, well-researched, and sold with a standardized concentration of monocolin K (lovastatin). Eventually, this product was legally deemed a drug, as opposed to a dietary supplement, and thus is no longer sold over the counter as a “standardized” compound. Despite the theoretical advantages of synergistic blends of natural statins, there is an inherent uneasiness about prescribing a product with extreme lot-to-lot and product-to-product variations. A recent analysis of available, off-the-shelf RYR products revealed a range of 0 to 20 mg lovas-

tatin per capsule, depending on the brand purchased. In addition, several RYR products were found to contain high levels of citrinin, a contaminating mycotoxin that has been linked to nephropathy.

As with any therapy, supplements should be researched prior to recommending them to patients. Although there is a lower incidence of reported myopathy with the RYR compounds relative to pharmaceutical doses of statins, the standardization of dosing and the screening for contaminants of pharmaceutical statins can make these (especially at the safer lower doses) a more attractive form of cholesterol management than the present day RYR compounds.

Coenzyme Q10 (ubiquinone) is a mitochondrial protein that is essential to the electron transport cycle. In addition to its role in cellular energy production, CoQ10 also acts as a potent antioxidant. Of cardiovascular relevance is the biochemistry of statin activity and the subsequent effect of statins on CoQ10 levels. The mevalonic acid biochemical pathway is mediated by HMG-CoA reductase and is inhibited by statin drugs and yields both cholesterol and CoQ10. Inhibition of HMG-CoA reductase by statins (and perhaps beta blockers) lowers endogenous CoQ10 levels.

In the body, CoQ10 is highly concentrated in muscle cells—both skeletal and cardiac—with their high mitochondrial content. The idea of using CoQ10 supplements to correct this deficit gained considerable appeal following the publication of several studies that described marked decreases in statin-induced myopathy when CoQ10 was administered concomitantly with the statin. Additionally, CoQ10 supplementation may prevent or alleviate statin-associated

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congestive heart failure. Furthermore, CoQ10 has been shown to lower blood pressure in several studies, as well as to improve function in patients with Parkinson's disease. Serological measures of CoQ10 concentrations in blood or tissue are fraught with technological difficulties, so such tests are not routinely recommended. Doses are usually in the range of 30 to 200 mg daily (higher in cases of Parkinson's disease); absorption may be improved if taken with a fatty meal.

Phytosterols are often ignored in the United States but have retained a high popularity in Europe. Plant sterols and stanols are typically taken orally 15 to 30 minutes before meals. The structural similarity to animal sterols (i.e. cholesterol) allows these compounds to saturate the intestinal receptors, competitively preventing absorption of animal cholesterol from meals. The overall effect of such a phytosterol regimen is a decrease in total and LDL cholesterol levels. While capsules are preferred in the United States, there are many foods and beverages available that incorporate plant-derived sterols and stanols.

Several brands of margarine that are rich in these compounds are available but must be taken regularly. Typical dosing is 0.8 grams of phytosterols taken twice daily prior to meals.

There are numerous reliable sources of additional information for busy clinicians. Most mobile purveyors of conventional medical information have added sections that deal with over-the-counter botanicals and supplements. In addition, there are several dedicated online sites that are excellent sources of such information. Natural Medicine Comprehensive Database (<http://naturaldatabase.therapeuticresearch.com>) and Natural Standard (www.naturalstandard.com) are two such resources (subscriptions required). The information is clear, highly referenced, and frequently updated. In addition, drug interactions are included where applicable, and even hypothetical interactions are presented. Finally, a graded effectiveness level is included on both sites.

Recommendations of high-quality brands of a dietary supplement or botanical are complicated by the fact that these agents are classified as "di-

etary supplements" and are thus not regulated like pharmaceuticals. There are a few methods available to the clinician to identify high-quality products or to verify the correct chemical and amount. One resource is Consumerlab.com (www.consumerlab.com), which assays select products for accurate amounts and the presence of contaminants. Access to their website is by subscription. Some manufacturers use independent assay labs, such as the United States Pharmacopeia (USP) or the National Sanitation Foundation (NSF). These organizations certify products for purity and accurate tablet ingredient concentrations and then allow the manufacturer to display the "USP" or "NSF" endorsement on the product label. Lists of certified products are available online.

The use of dietary supplements and botanicals is increasing to the point that the internist can no longer ignore it. Some focused review will allow the clinician to gain enough familiarity with these compounds to engage in meaningful conversation with patients and provide more reliable counsel.

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