Dietary supplements and *The American Journal of Clinical Nutrition*[1,2]

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What to do about manuscripts that deal with dietary supplements? Are studies on herbs and other botanicals eligible for inclusion in a journal that focuses on clinical nutrition? First, here are some definitions. According to the Dietary Supplement Health and Education Act (DSHEA) of 1994, *dietary supplements* are products "intended to supplement the diet to enhance health," and include vitamins, minerals, amino acids, herbs, and other botanicals. A dietary supplement is "not represented as a conventional food or a sole item of a meal or the diet." In a recent Forum section of *Science*, Zeisel (2) defined a *neutraceutical* as "a diet supplement that delivers a concentrated form of a biologically active component of food in a non-food matrix in order to enhance health." Dietary supplements and neutraceuticals are distinct from *functional foods*, which deliver an active ingredient within the food matrix, and *food additives*, which enhance flavor or aroma but not the nutritional value of a food.

It is estimated that more than 40% of Americans take some form of dietary supplement, about half as herbals, with a total market value greater than $12 billion in 1998, nearly double the 1996 value (3). An informal survey of patient and physician attitudes highlighted the widespread use of herbals and other unconventional remedies among arthritis patients, most of whom derived their advice from the Internet. In addition, many physicians are beginning to meet the perceived needs of their patients by designing so-called integrative practices that incorporate supplements into their treatment regimens (4).

Yet, there are troubling aspects of this turn of events. Dietary supplements and neutraceuticals are subject to a different efficacy and safety standard than are pharmaceuticals and functional foods, even though they may share the goal of enhancing health. The DSHEA, approved by the US Congress in 1994, was designed to facilitate public access to "natural" medicines. The Act assumes that all dietary supplements marketed before October 1994 are safe, whereas new supplements can be marketed with only the manufacturer's assurance of safety, bypassing the usual procedures of the Food and Drug Administration (FDA) that require proof of safety for public consumption of pharmaceuticals (1, 2, 5).

Dietary supplements are usually marketed to ameliorate symptoms or to address systemic conditions, and the only real DSHEA prohibition is the labeling of dietary supplements as disease specific. Manufacturers need not list the amounts or exact composition of ingredients (6). The medical literature is rife with reports of unsuspected toxicities from unregulated dietary supplements. These include reported toxic effects from cardiac glycoside contamination of plantains promoted for "intestinal cleansing" (7), increased estrogenic clinical effects from use of an herbal product marketed for "improvement of the immune system" in patients with prostate cancer (8), and undeclared potentially toxic drugs or heavy metals in one-third of Asian patent medicines in California (9).

As discussed in a recent editorial, the liver is the target organ of many toxic chemicals found in plants that have evolved complex mechanisms for inflicting hepatocellular injury as survival strategies against animals (10). Thus, gullible human consumers of untested herbal products may put themselves at risk by exposure to normal processes of plant evolution. All these troubling data point to the imperative for well-designed, comprehensive studies on the proper medical use of neutraceuticals and other dietary supplements before these products become ingrained in medical practice without clear knowledge of their mechanisms, clinical efficacy, and safety.

The American Journal of Clinical Nutrition (*AJCN*) Editorial Board discussed these realities and concerns with the goal of developing policy guidelines on the acceptability of papers that focus on the use of dietary supplements. Although botanicals are traditionally the foundation of pharmacology, we concluded that their widespread use as dietary supplements supports their inclusion in the realm of clinical nutrition. Furthermore, we believe that the application of objective peer review and the *AJCN*'s standards of scientific excellence will serve future authors and readers of articles on nutritional supplements. However, editorial caution is required to ensure that submitted papers meet high ethical standards. Currently, the food-supplement industry's marketing enthusiasm fuels a burgeoning investment in product testing in vitro, in animal models, and in human subjects. Yet many studies on dietary supplements are funded by the very companies whose marketing fortunes rest on the scientific approval of their products. With these concerns in mind, the editors developed the following guidelines for considering papers on dietary supplements.

As is the case for all *AJCN* submissions, papers that deal with a product that falls within the category of dietary supplements will undergo initial review by at least 2 members of the Editorial Board, who will then advise the Editor on the suitability of the manuscript for subsequent full peer review by using the criteria of scientific excellence, comprehensiveness, and relevance to the field of clinical nutrition. For example, papers that deal

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with only in vitro studies of a compound or substance will be considered to be within the realm of food science unless they clearly contribute to the understanding of a clinically relevant mechanism. Similarly, papers that report only on the bioavailability of a compound or substance may be viewed as too limited in scope for the *AJCN*. A paper that focuses on a botanical in capsule form for treatment of a nonnutritional disease may be recommended for resubmission to a pharmaceutical journal.

By contrast, comprehensive papers concerning the clinical use of a dietary supplement in the context of diet or a diet-related disease would be viewed as appropriate for the *AJCN*. Ideally, such papers would report on a well-controlled clinical trial with adequate numbers of experimental subjects that examined data on the biological effect and bioavailability of the compound or substance under study. These papers must address the usefulness of the dietary supplement in the context of health benefit or disease prevention and must provide substantial data on efficacy and potential toxicity. The contents of the dietary supplement under study must be listed in quantitative detail. Even though the dietary supplement in question may not have met stringent FDA standards for approval, the *AJCN* will require assurance in the body of the manuscript that the safety issue has been adequately addressed and approved by the relevant institutional review board in full accordance with the Declaration of Helsinki (11). The Editors will consider review papers on dietary supplements or neutraceuticals eligible for peer review and potential publication if they are found to be both comprehensive and balanced, to deal with all issues of biological and clinical efficacy and safety, and to be of significance to the field of clinical nutrition. Authors of original and review articles must list their sources of funding in a footnote to the title, and the cover letter must disclose potential conflicts of interest such as membership of the advisory board of the funding source.

In summary, the *AJCN* Editors consider that papers on dietary supplements that meet our standards of ethics and scientific excellence are within the purview of the *AJCN*. The Editor and Editorial Board expect that authors of these papers will pay close attention to these standards in the conduct of their research and in their decision to submit to the *AJCN*.

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The American Journal of Clinical Nutrition