REVIEW ARTICLE

Integrating Herbs and Supplements in Managed Care: A Pharmacy Perspective

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Abstract

Herbal and other dietary supplements are popular among patients. Whether and how to establish and manage an herbal formulary remains a challenge for conventional managed-care organizations. Pharmacists and clinicians depend on evidence-based guidelines to help determine which products (whether pharmaceutical or herbal) to make available to patients. Evidence from randomized controlled trials that supports the use of most herbal supplements is scarce, yet for some supplements, credible evidence supports the possibility of efficacy. Quality control remains of concern for the supplement industry and for patients and clinicians considering the use of supplements.

Clinicians may improve care by both disseminating educational materials and making available to patients popular quality-controlled herbal supplements deemed safe and effective. Kaiser Permanente Northwest (KPNW) has adopted a comprehensive and systematic approach to managing and stocking herbal supplements that can serve as a model for other conventional and managed care organizations.

KPNW's dedicated Natural Products Advisory Committee (NPAC) has made considerable progress toward developing a constructive response to KPNW patients' herbal supplement use. Making supplements available at pharmacies can improve clinical outcomes, patient convenience, and quality control. NPAC currently limits its reviews to randomized, controlled trials and data from meta-analyses and systematic reviews for single-ingredient supplements. As interest in this area maintains steady growth, NPAC will continue to study how best to meet patients' needs.

Background

Herbal and other dietary supplements are popular among patients.[1] Whether and how to establish and manage an herbal formulary remains a challenge for conventional managed care organizations. Pharmacists and clinicians justifiably desire to adhere to evidence-based guidelines in determining which products (whether pharmaceutical or herbal) to make available to patients. Evidence from randomized controlled trials that supports the use of most herbal supplements is scarce, yet there are some supplements for which there is credible evidence that supports the possibility of efficacy.[2,3] In some instances such "proven" products are popular among patients and are recommended by many clinicians. Quality control remains a perplexing problem for the supplement industry,[4] however, and patients can have a difficult time recognizing and identifying high-quality products.

The issue is further complicated by the fact that complementary and alternative medicine systems such as Ayurveda[5] and Traditional Chinese Medicine indicate the prescription of multi-ingredient herbal

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mixtures. Such mixtures may have a long history of use but are difficult for the health care industry to evaluate, comprehend, and standardize.

Given this complex array of issues, the prevailing confusion about herbal supplements within conventional health care comes as no surprise. Against such a backdrop, we may improve care both by disseminating educational materials and by making available to patients those popular, quality-controlled herbal supplements deemed safe and effective. Kaiser Permanente Northwest (KPNW) has adopted a comprehensive, systematic approach to managing and stocking herbal supplements that can serve as a model for other conventional and managed care organizations.

In 2000, the KPNW Regional Formulary and Therapeutics Committee (RFTC) established the dedicated Natural Products Advisory Committee (NPAC). NPAC, charged with the mission of providing "information and advice to the RFTC about natural products," is an interdisciplinary committee of pharmacists, clinicians, and dietitians. NPAC evaluates which products to stock and leverages organizational systems, including the electronic medical record (EMR), as tools for educating clinicians and patients about herbal supplements.

Guidelines for Assessing Natural Products

NPAC developed a set of four criteria to provide a framework for determining which natural products to stock at KPNW over-the-counter pharmacies:

1. Is there sufficient evidence from randomized controlled trials to suggest efficacy?
2. Are there significant concerns regarding product safety and drug–herb interactions?
3. Is a high-quality product available?
4. Is there sufficient interest in the supplement among patients and/or clinicians?

The Role of Evidence-Based Medicine

Evidence-based medicine (EBM) has been defined as the "set of principles and methods intended to ensure that to the greatest extent possible, medical decisions, guidelines, and other types of policies are based on and consistent with good evidence of effectiveness and benefit."[6] As more and more natural products on the market make their way into conventional medicine, NPAC provides high-quality evidence reviews to guide clinicians, pharmacists, and patients in making informed decisions regarding whether to use these supplements.

Prior to reviewing a product, NPAC formulates a clinical question in collaboration with primary and/or specialty care clinicians, pharmacists, and our EBM team of specialists (MD methodologists and consultants). This step is critical. Many supplements are commonly used for a range of indications, but the clinical question(s) must be narrowly defined to make an evidence review feasible. The clinical question emphasizes outcomes and typically addresses potential benefits and harms of the intervention or supplement being investigated.

In carrying out a critical appraisal of the literature, NPAC follows quality parameters set forth by the EBM team. The methodology includes a thorough and systematic search of the literature using high-quality electronic databases, including natural-product databases, Cochrane, PubMed, and Ovid. Ideally, NPAC focuses on relevant systematic reviews and meta-analyses first. Then, the EBM consultant and the methodologist identify, critically appraise, and score all other relevant experimental and epidemiologic studies assessing the efficacy of the supplement in question. From this rigorous process, NPAC creates an evidence synopsis to ensure that resulting recommendations are reliable and relevant. The EBM team brings clinical expertise and training in epidemiology to formulate recommendations that are based on the quality of the evidence. The evidence synopsis documents the search-and-appraisal process, including search terms and databases used, and all other Kaiser Permanente (KP) content informed by the synopsis. It also serves as the primary template for updating content on an annual basis and for necessary revisions when new and landmark studies are released.

Quality Control and Vendor Selection

When NPAC determines, on the basis of evidence, that a dietary supplement is effective and safe, NPAC looks for a quality product to make available for sale in KPNW pharmacies. Currently, there is no effective governmental oversight of herbal supplements or assurance of product integrity. Newly crafted rules could provide the Food and Drug Administration (FDA) with more rigorous oversight authority beginning as early as 2008.[7] Ultimately, the supplement industry must do a better job of manufacturing and certifying dietary supplements that are consistently free of contamination and accurately labeled.

Supplement manufacturers in the US may participate in voluntary quality-certification programs, including the US Pharmacopoeia (USP) verification.[8] USP verification ensures that supplements are

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tested for the following:

1. The label accurately lists what is in the bottle—all the listed ingredients are present in the declared amount.
2. The supplement does not contain harmful levels of contaminants.
3. The supplement will break down and release ingredients in the body.
4. The supplement has been made under acceptable manufacturing practices.

Unfortunately, USP verification of herbal supplements is not widespread, leaving purchasers to try to identify quality-controlled manufacturers and products. NPAC provides this important service for KPNW patients, who as individuals may lack the time, resources, and expertise to properly identify and research the issues. When USP-verified products are not available, NPAC requires that the vendor provide a certificate of analysis as documentation of product content and purity. Currently, the KP nationally contracted National Vitamin Company's Nature's Blend line provides quality-controlled supplements for our pharmacies at a competitive price.

Specific Supplements

Products that have been reviewed and are currently in stock at KPNW pharmacies include St John's wort[8] for symptomatic relief of mild to moderate depression; saw palmetto[9] for urinary symptoms related to benign prostatic hyperplasia; glucosamine sulfate[9] for pain related to osteoarthritis; gingko biloba[10] to improve memory and attention in patients with cognitive impairment; omega-3 fatty acids,[11] as in fish oil and flaxseed oil, for high triglyceride levels and secondary prevention of ischemic heart disease; and melatonin[12] for jet leg and insomnia.

NPAC has taken a neutral stance regarding a number of popular natural products that, although likely safe, have insufficient evidence regarding efficacy, including black cohosh[13] for menopausal hot flashes; coenzyme-Q_{10}[14] for neurologic disorders and prevention of statin-induced myalgias; echinacea[15] to prevent or ameliorate cold and flu symptoms; feverfew[16] for migraine prophylaxis; and garlic[17] for cardiovascular indications. In such cases NPAC has commonly advised pharmacies against stocking the product but may assemble handout and informational materi-

The Herbal Pharmacy Marketplace

Tieraona Low Dog, MD

This article is an absolute must read for hospital pharmacies, administrators or clinicians looking to stock and sell dietary supplements, including herbal products. There is little question that the marketplace for herbal products continues to grow at a steady pace. Indeed, between 1990 and 1997, use increased by 380% in the US.[1] In fact, when looking across all complementary and alternative practices, the greatest relative increase in the US between 1997 and 2002 was herbal medicine (12.1% vs.18.6%, respectively; representing 38 million adults).[2] There are thousands of herbal products being sold in the marketplace, including a considerable number of dubious efficacy, uncertain safety, and/or questionable quality making it almost impossible for the consumer to discern the good from the bad, the effective from the ineffective, or the safe from the dangerous.

Results from scientific studies are lost in the storm of information available on the Internet and in the mass media, where pseudoscientific and misleading promises are intermingled with factual and promising information that could improve the health of our patients. Whereas quality should definitely improve in the coming years due to the Food and Drug Administration's issuance and enforcement of the new good manufacturing practices for dietary supplement manufacturers (cGMPs), there will continue to be problems in the short term and challenges will remain for products being imported from Asia and the Indian subcontinent. In a review of safety risks, it was noted that "many of the cases where herbal products have been associated with actual human poisoning were not in fact caused by herbs alleged to be in the product, but resulted from substitution or contamination of the declared ingredient, intentionally or by accident, with a more toxic botanical, a poisonous metal, or a potent nonherbal drug substance."[3] Adulteration with prescription medications remains a concern for a number of traditional Chinese medication products.[4] There is no question that high-quality products must be the first step in guiding patients' decisions regarding dietary supplement use.

It is unreasonable to assume that average consumers will be able to easily identify a high-quality product that is evidence based for their specific

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als to guide clinicians and patients in the context of evidence-based shared decision making.

Notable product rejections by the committee have included Airborne, Avlimil, kava, and ephedra. Airborne, promoted for prevention of respiratory illness, was identified as ineffective. Avlimil, purported to enhance "female libido," has not been shown effective and has been cited as a possible cause of pancreatitis.[18] Other products were rejected consistent with FDA bans against their use. Kava has been associated with liver injury.[19] Ephedra,[20] once a common ingredient in weight-loss formulas and energy supplements, was banned by the FDA as of April 12, 2004, because of its links with hypertension, myocardial infarction, seizures, stroke, and death.

Many KP regions other than KPNW maintain processes for evaluating and stocking herbal supplements. Comparison (Table 1) reveals substantial though not complete concordance among regional pharmacy experts.

Documentation and Education

Integration with the EMR

It is essential that clinicians can document in the medical record when patients are using herbal products and that there are tools to guide both the clinician and the patient to safe and effective care. The EMR used at KP is a flexible tool that can be modified to serve these needs. Because all clinicians share the same EMR, the detailed information about an individual's supplement use is accessible wherever the patient may interact with the health system. The EMR also serves as an interactive tool in the examination room, allowing clinicians to display graphs of blood pressures and trends in laboratory results and to share clinical practice guidelines and reference materials from the KPNW Intranet. The EMR can also serve as a safety tool that allows automatic checking for interactions between drugs and natural products at the moment of order entry. The KP EMR did not come loaded with all of these tools built in; the clinicians of KP, with guidance from NPAC, have modified the system to make it work for their needs.

Three key features have been developed in the EMR regarding use of natural products: documentation, decision support, and patient safety.

condition, and know the dosage, duration of use, and possible interactions with other medications. Thus, it is imperative that patients have a trusted, nonbiased and authoritative voice that can help them make informed decisions regarding supplement use. In addition to the physician, it should also include the pharmacist, a member of the health care team who is critically important in this regard, but definitely underutilized. Pharmacies can offer patients a selection of high-quality, evidence-based dietary supplements on-site that will allow pharmacists to counsel patients about their use and provide information about safety and possible herb-drug interactions, as well as adding to patient convenience. The Natural Products Advisory Committee (NPAC), as described by Elder et al, has created a reasoned criteria for determining product and vendor selection, allowing them to stock a number of supplements such as omega 3 fatty acids, saw palmetto, and St John's wort in the Kaiser Permanente Northwest (KPNW) pharmacy. It has also been able to reject products that have questionable effectiveness, possible safety concerns, or both. As an interdisciplinary committee, it is composed of pharmacists, dieticians, and clinicians who have been able to leverage organizational systems, such as the electronic medical record (EMR), to serve as tools for educating both patients and clinicians. Handouts save clinicians' time and provide a much-appreciated service for patients. Including a place to record supplement and medication use in the EMR is critical for monitoring and reporting adverse event reporting, something that is unfortunately grossly inadequate in the health system at large.

I highly commend KPNW for their foresight in meeting this critical public need. I also commend the NPAC, who have worked hard to create a responsible tool for educating patients and clinicians, for sensible integration of supplement use into the EMR, and for a thoughtful approach to product and vendor selection for stocking their pharmacy. Hopefully, it can serve as a model for others to do the same! ❖

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Table 1. Supplements stocked across five Kaiser Permanente regions

Supplement	Indication	Northwest	Northern California	Colorado	Southern California	Hawaii
St John's wort	Depression	X	X	X	X	X
Glucosamine (chondroitin)	Osteoarthritis	X	X	X	X	X
Gingko Biloba	Cognitive impairment	X	X	X	X	X
Omega 3/fish oils	Lipids	X	X		X	
Melatonin	Jet lag	X	X		X	
Flaxseed	Lipids	X				
Saw palmetto	Prostatic hypertrophy	X	X		X	X
Echinacea	Upper respiratory infection		X	X	X	X
Probiotics	Rotaviral diarrhea		X		X	
Garlic	Atherosclerosis			X		X
Coenzyme Q_{10}	Parkinson disease					X
Feverfew	Migraine					X
Ginger	Nausea					X
Milk thistle	Liver dysfunction					X

X indicates supplements that are stocked in this Region

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Documentation

For complete clinical understanding of an individual patient, it is essential to document what medications or natural products the patient is taking and why. In the KP EMR, clinicians can record a patient's use of a particular supplement on the medication list by entering the supplement name as an order and then associating the order with a specific diagnosis. Alternatively, if the clinician enters *Herbal* in the orders field, a drop-down list of supplements will appear (Figure 1).

Decision Support

Once the clinician selects the relevant product, brief synopses regarding indications, dose, efficacy data, and side effects will pop up for the clinician to review (Figure 2). The program provides links to additional Web-based resources, including:

- Relevant KPNW clinical practice guidelines
- The NPAC-sponsored evidence synopsis
- Pertinent monographs from the Natural Medicines Comprehensive Database
- The NPAC-authored *Dr Herbal* clinician newsletter
- An NPAC-authored patient handout.

Patient Safety

Drug–herb interactions and herb-allergy alerts will appear as a pop-up to alert clinicians when entering certain supplements.

Patient Education and Marketing

KPNW pharmacies consistently stock only those supplement products approved through the processes outlined above. NPAC frequently selects products for review on the basis of clinician or pharmacist request, which in turn may be patient driven. The addition of a newly approved supplement to our shelves is not accompanied by any direct patient promotion or advertising. Table 2 details actual product sales for seven stocked natural products at KPNW pharmacies for the 12-month period July 2006 through June 2007, based on a service population of about 470,000 patients.

NPAC devotes considerable energy to developing patient-education handouts for selected herbal products, including those in KPNW pharmacies and other commonly used supplements. Patient-education handouts are primarily requested and printed at KP pharmacies but

Table 2. 12-month product sales at Kaiser Permanente Northwest pharmacies

Supplement	Dose (mg)	Form of supplement	Bottles sold
Omega-3	1000	#90	3729
Flaxseed	1000	#90	1480
Gingko biloba	40	Capsule #60	333
Glucosamine sulfate	500	Capsule #60	2392
Melatonin	3	Tablet #60	1955
Saw palmetto	160	Tablet #30	1078
St John's wort	300 mg	Capsule #60	518

can also be printed on demand from examination-room computers and other designated patient-education environments. Being able to provide this resource at the point of care allows KP to provide patients with valuable information on dosing, side effects, drug–herb interactions, and cost. When necessary, NPAC will prepare handouts for supplements that raise significant patient safety concerns, such as kava and ephedra.

KPNW pharmacists provide patient education during face-to-face encounters regarding supplement use. The most common patient inquiries at the pharmacy relate to pricing and herb–drug interactions. Frequently, patients present to the pharmacy with a product purchased elsewhere and inquire whether they can take it concurrently with their prescribed medications. Pharmacists can screen for drug–herb interactions using the electronic dispensing system and can access a variety of additional online resources, including the Natural Medicines Comprehensive Database and Natural Standard.

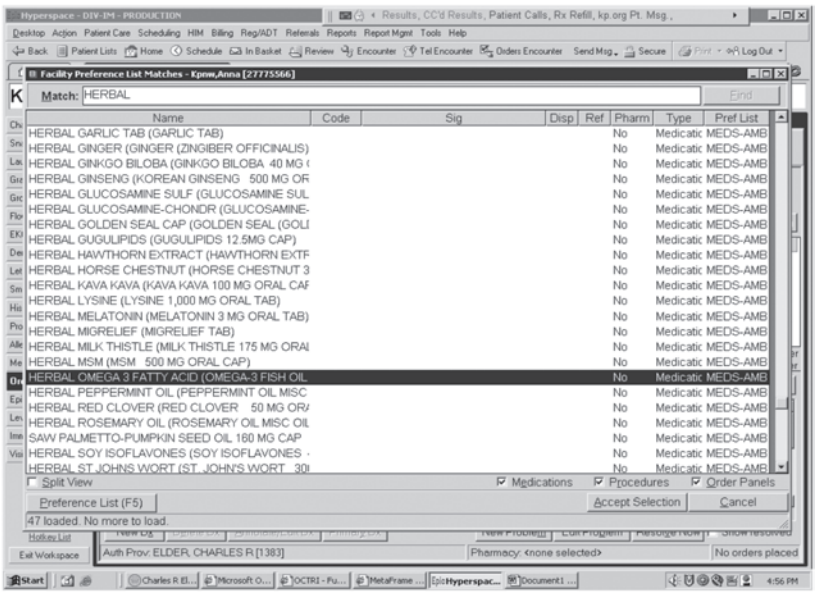

Figure 1. Kaiser Permanente electronic medical record drop-down list of supplemental products.

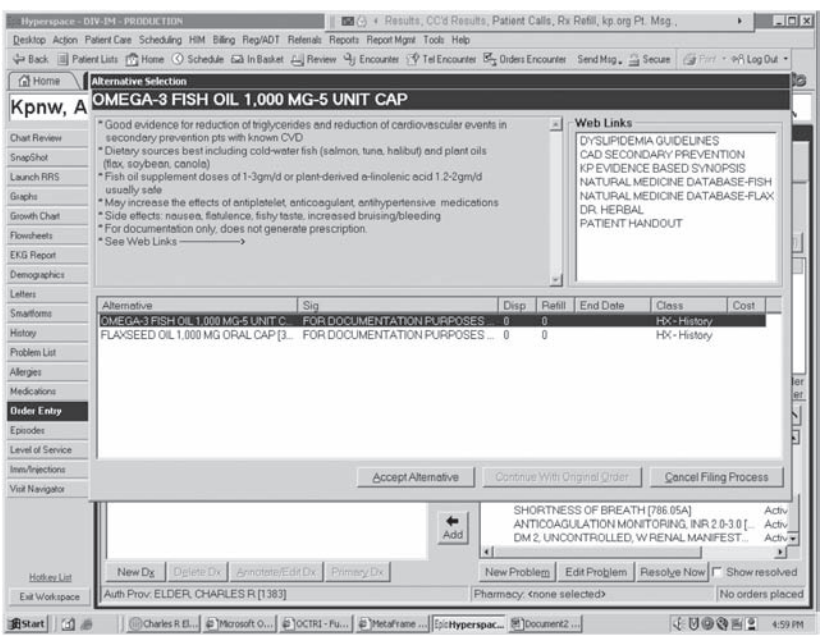

Figure 2. Brief synopses regarding indications, dose, efficacy data, and side effects, along with links to additional Web-based materials, can be accessed for individual products.

Conclusion

NPAC has made considerable progress toward developing KPNW's constructive response to our patients' herbal supplement inquiries and use. It is sensible for a managed care organization such as KPNW to make quality supplements available at pharmacies, from the standpoints of clinical outcomes, patient convenience, and quality control. Currently NPAC generally limits its reviews to randomized controlled trials and data from meta-analyses and systematic reviews for single-ingredient supplements. We recognize, however, that the popularity of herbal therapies and alternative medicines extends to teas, spices, traditional multi-ingredient herbal mixtures, and other food products, especially among some ethnic populations. As interest in this area maintains steady growth, NPAC will continue to study how best to meet patients' needs. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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It Was Good

And the earth brought forth grass, and herb yielding seed after his kind, and the tree yielding fruit, whose seed was in itself, after his kind: and God saw that it was good.

— Genesis 1:12, The Bible, King James Version