

ACCP WHITE PAPER

White Paper on Natural Products

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The American College of Clinical Pharmacy (ACCP) published an initial white paper on herbal products in 2000. Since then, the global market for natural products has continued to expand, with tens of millions of consumers using such products on an annual basis in the United States alone. However, despite this expansion, natural products remain largely unregulated compared with prescription medications, have moderate- to low-level clinical evidence for efficacy, and continue to have safety concerns, including adulteration and misbranding. As comprehensive medication management experts, clinical pharmacists are uniquely qualified to navigate these concerns and advise patients appropriately. To develop and recommend a suitable care plan involving natural products, clinical pharmacists must establish a strong pharmacist-patient relationship, assess the appropriateness of therapy, educate the patient regarding key issues, and continuously monitor and follow up on the effectiveness of the care plan. This process should not only occur in an individual community or hospital setting, but also whenever a patient transitions from one care setting to another in cooperation with other clinicians.

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The U.S. market for natural products continues to expand, even though the clinical evidence to support the effective and safe use of many of these products is still limited. In 2000, the American College of Clinical Pharmacy (ACCP) published a white paper on herbal products that

recognized the emerging role of natural products as a common self-care therapy among patients and the need for pharmacists to actively embrace the responsibility for educating individuals on their appropriate use.¹ The current white paper on natural products replaces the 2000 document and discusses regulatory issues, provides a brief overview of the efficacy and safety evidence regarding natural products, reviews contemporary natural product resources, and provides recommendations for the clinical pharmacist on how to incorporate natural products into medication histories and medication reconciliation, transitions of care, and discharge planning. In addition, this paper recommends a process for clinical pharmacists with respect to educating patients specifically on the use of natural products. The scope of this paper is limited to a discussion of natural products and does not include homeopathy, traditional Chinese medicine, medical marijuana, or caffeine supplement products.

According to the National Center for Complementary and Integrative Health, the term *natural products* includes a diverse group of substances

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that are produced by marine organisms, bacteria, fungi, and/or plants.² The term includes extracts from the aforementioned “producers,” isolated compounds derived from these extracts, and vitamins, minerals, and probiotics. Many natural products are widely available and marketed to consumers as dietary supplements. A dietary supplement is defined by the U.S. Food and Drug Administration (FDA) as a product intended for ingestion that contains a dietary ingredient intended to add further nutritional value to the diet.³ Patients and clinicians may use a variety of other terminology interchangeably when discussing natural products, including herbals, botanicals, supplements, alternative, and complementary.

Consumers continue to embrace natural products. It is estimated that they will spend \$115 billion on herbal supplements globally by 2020.⁴ In 2014, consumers spent around \$6.4 billion on herbal supplements in the United States.⁵ This represents a 6.8% increase over 2013 and the 11th consecutive year of increased market growth. However, although sales of natural products have increased steadily, results from the National Health Interview Survey (NHIS) indicate that the percentage of individuals who have ever taken a natural product actually decreased from 2002 (25.1%) to 2012 (23.6%), with an estimated 40 million adults stating they had used a natural product in the past 12 months.⁶ Further analysis of the NHIS data reveals that factors associated with natural product use include being 45–64 years of age, being uninsured, being of the female sex, having a higher education, living in the western part of the United States, using over-the-counter medications, and choosing “non-Hispanic other” as race.⁷ In addition, a survey of practices at 29 centers for integrative medicine affiliated with a hospital, health care system, and/or medical or nursing school revealed that natural products are commonly recommended by clinicians for various chronic and acute conditions.⁸ More than 20 centers reported using natural products to treat allergies, arthritis, chronic pain, depression, fatigue, gastrointestinal disorders, headache, and stress.

Regulation

The FDA regulates many natural products through a set of regulations separate from those used for conventional medications.⁹ Under the Dietary Supplement Health and Education Act of

1994 (DSHEA), manufacturers and distributors are prohibited from marketing products that are adulterated or misbranded, whereas the FDA is responsible for enforcement actions against any product that is already marketed and found to be adulterated or misbranded.^{9, 10} Clinical pharmacists should be aware of federal regulatory issues and advise patients regarding the following, if needed¹¹:

- DSHEA requires that all natural products classified as dietary supplements be labeled with either the term *dietary supplement* or a similar term (e.g., herbal supplement or iron supplement).
- Dietary supplements do not require FDA approval and are not required to be proven effective or safe before marketing, which is in contrast to the approval process for conventional medications.
- For most labeling claims of dietary supplements, federal law does not require the manufacturer or distributor to prove to the FDA that the claim is accurate before marketing the product.
- Marketing of a dietary supplement for the treatment or cure of a disease, or to specifically alleviate the symptoms of a disease, is illegal (e.g., a dietary supplement label may not state that it “cures diabetes,” but it may state that the product “positively affects blood glucose levels”).
- Once a dietary supplement is available for purchase to consumers, the FDA monitors mandatory reporting of serious adverse events potentially related to the use of these products by manufacturers or distributors as well as voluntary adverse event reporting by consumers and clinicians. In addition, the FDA may review package inserts, product labels, and other material as resources permit to ensure that misbranding does not occur.

Unlike the evaluating of claims made within the product labeling, evaluating the integrity of claims made in dietary supplement advertising (print and broadcast ads, infomercials, and direct marketing materials) does not fall to the FDA but to the Federal Trade Commission (FTC), although both agencies work closely to ensure the consistency of enforcement efforts.^{11, 12} Application of FTC law to dietary supplement advertising may basically be summarized in two statements. First, all advertising related to the product must be truthful and not

misleading.¹² Second, advertisers must have adequate data (competent and reliable scientific evidence) to substantiate all objective product claims before an advertisement is disseminated for that product. When evaluating the health claims of these products within advertising, the FTC initially identifies all express and implied claims and then evaluates the scientific evidence to determine whether the data provide adequate support for the claim. The FTC gives great deference to an FDA determination of whether there is adequate support for a health claim, and usually, both agencies arrive at similar conclusions when assessing unqualified health claims.

Although natural products are not regulated like conventional medications, many such products do follow current good manufacturing practices (CGMPs) and may be taken safely by patients. In 2007, the FDA announced a final rule that established regulations requiring CGMPs for dietary supplements, including ensuring quality throughout the manufacturing, packaging, labeling, and storing processes.¹³ This rule also discusses requirements for quality control procedures, design and construction of manufacturing facilities, recordkeeping, handling of consumer complaints, and testing of ingredients and final products. The goal of this rule is to establish CGMPs industry-wide to ensure that dietary supplements are manufactured consistently with respect to identity, purity, strength, and composition. In addition, independent organizations analyze the quality of natural products that are voluntarily submitted. These include the

United States Pharmacopoeia (USP) and the National Sanitation Foundation (NSF). United States Pharmacopoeia-verified products are evaluated to ensure that what is stated in the label is what is in the bottle in the declared potency and amounts, that the product does not contain harmful levels of certain contaminants, that the product will be metabolized and eliminated from the body within a specified time, and that it is manufactured according to the FDA's CGMPs.¹⁴ The NSF certification process includes a toxicology and label review to verify product formulation and labeling claims, a formulation review that ensures that what is on the product label is actually in the product, contaminant testing, and a CGMP facility inspection.¹⁵ Because of issues related to efficacy and safety as discussed in the text that follows, clinical pharmacists should recommend USP-verified or NSF-certified products to patients, whenever possible.¹⁶

Beyond the federal level, some states also regulate aspects of natural products. For example, California has specific regulations that require warnings on dietary supplements that contain stimulant laxative ingredients (e.g., senna, cascara sagrada, aloe latex, rhubarb root).¹⁷ Clinical pharmacists should be aware of applicable regulations within their state of practice, many of which may be identified through state Department of Public Health (or equivalent agency) websites. Table 1 provides an overview of the key agencies and independent organizations involved in the regulation of natural products.

Table 1. Overview of Natural Product Regulation

Agency/Organization	Overview	Online Resources
U.S. Food and Drug Administration (FDA)	<ul style="list-style-type: none"> Federal agency primarily responsible for enforcement actions against already marketed products that are misbranded or adulterated Monitors mandatory reporting of serious adverse events from manufacturers Monitors voluntary adverse event reporting by consumers and clinicians Reviews package inserts, product labels, and other material to ensure that misbranding does not occur 	FDA dietary supplements FDA 101: dietary supplements (for consumers) FDA current good manufacturing practices (CGMPs) for dietary supplements
Federal Trade Commission (FTC)	<ul style="list-style-type: none"> Federal agency that evaluates the integrity of claims made in product advertising Works closely with the FDA to ensure consistency in enforcement efforts 	FTC dietary supplements: an advertising guide for industry FTC dietary supplements – consumer information
United States Pharmacopoeia (USP)	<ul style="list-style-type: none"> Independent organization that verifies the quality of natural products that are voluntarily submitted 	USP-verified dietary supplements
National Sanitation Foundation (NSF)	<ul style="list-style-type: none"> Independent organization that certifies the safety of natural products that are voluntarily submitted 	NSF dietary supplement safety

State of the Evidence

Efficacy

Systematic reviews (with homogeneity) of randomized controlled trials (RCTs) represent the strongest level of evidence for therapeutic interventions, whereas expert opinion is the weakest and lacks the ability to reach conclusions regarding medication efficacy.¹⁸ Clinical pharmacists should be aware that many natural products have moderate- to low-quality clinical evidence for efficacy, with few products evaluated in appropriately designed clinical trials. The 10 most commonly used natural products among adults in 2012 were fish oil/omega-3 fatty acids, glucosamine/chondroitin, probiotics/prebiotics, melatonin, coenzyme Q₁₀, *Echinacea*, cranberry, garlic, ginseng, and ginkgo biloba.¹⁹ These natural products have a mixed quality of RCT evidence. The quantity of trials available for these products allows for characterizing the evidence available through systematic reviews and/or meta-analyses; however, clinicians must take great care when evaluating systematic reviews and meta-analyses to ensure that appropriate methodology is used and limitations are communicated.

Efficacy studies involving natural products are generally not as robust and rigorous as those required for prescription medications. These studies are further complicated by the fact that a natural product may not have the same consistent ingredients and quality among manufacturers.^{20, 21} A Consolidated Standards of Reporting Trials (CONSORT) statement published in 2006 provides a checklist of items necessary when reporting RCTs of herbal interventions.²² The checklist describes items commonly seen in RCTs for prescription medications; however, it also recommends a qualitative and quantitative description of natural product ingredients. Despite this recommendation, many trials may not conduct or adequately describe quantitative analyses for the natural product under examination.²⁰ In addition, the CONSORT statement is a recommendation, not a rule; therefore, researchers are not required to abide by its conventions. More compelling and robust trials on the efficacy of natural products are needed to better inform natural product use for patient care, and clinical pharmacists are encouraged to engage in research efforts to add to the body of clinical evidence regarding the efficacy of these products.

Safety

Historically, one of the main concerns regarding the safety of natural products was a lack of standardization and quality measures before marketing. Moreover, despite many reports of contamination and product substitution (i.e., an ingredient in the bottle different from what is on the label), this problem is ongoing.²³ In 2001, an Office of Inspector General report on dietary supplement adverse events found that 77% of products reported to the FDA lacked actual labels, and ingredients could not be determined for 32% of products.²⁴ In addition, adulteration, contamination, misidentification, and substitution of natural product constituents may occur. Published adverse events involving natural products are often in the form of case reports that include incomplete medical histories or lack product identification, which makes interpreting the actual adverse events secondary to the natural product suspect.

The FDA Adverse Event Reporting System contains information on the adverse events and drug error reports submitted to the FDA.²⁵ In 2013, the FDA received greater than 3000 adverse event reports related to dietary supplements, which resulted in hospitalizations, life-threatening illnesses, mortality, or other serious adverse events. This was 4 times the number of adverse event reports received in 2008. According to nationally representative surveillance data of U.S. visits to 63 emergency departments (EDs) from 2004 to 2013, an estimated 23,000 visits and 2000 hospitalizations occur annually secondary to adverse events related to dietary supplements.²⁶ Of the actual visits to EDs, 58.3% were female, and 28% involved young adults 20–34 years of age. Products most often implicated were for weight loss (25.5%), energy (10%), and sexual enhancement (3.4%). The most commonly reported adverse events were cardiac (palpitations, chest pain, or tachycardia). For patients 65 and older, choking or supplement-induced swallowing difficulty accounted for 37.6% of ED visits. Although cardiac symptoms predominated in the aforementioned study, other types of harm may occur. One such harm that is becoming increasingly apparent is liver toxicity. Increased marketing, lack of standardization, contamination, inappropriate use, and drug interactions are all likely causes of increased reporting of liver toxicity.^{27–29} Overall, adverse events related to natural products are dramatically underreported.²⁵ The many barriers

to adequate reporting of adverse events include lack of knowledge in how and where to report adverse events, fear of legal ramifications, uncertainty about causality, lack of time or incentive for reporting, and complacency. However, clinical pharmacists should strive to report adverse events related to the use of natural products using MedWatch or Natural MedWatch

Another major safety concern with using natural products is the potential for interactions with other medications. Research on natural product–drug interactions is often based on hypothetical possibilities because most published data involve *in vitro* and/or animal studies.³⁰ In addition, marketed natural products may include a mixture of bioactive ingredients with varying potency and purity, which can make it difficult to concretely identify the cause of an interaction.³¹ Similar to conventional medications, natural product–drug interactions have two main mechanisms—pharmacokinetic and pharmacodynamic. However, in contrast to most conventional medications, the exact mechanisms of natural product–drug interactions are not fully understood. The mechanism behind the bulk of known natural product–drug interactions involves oxidative metabolism by the CYP system (more than 78 dietary supplements potentially interact with this system) or effects on the

P-glycoprotein drug transporter.³¹ Natural products that contain hydrocolloidal fibers, gums, and mucilage may impair the absorption of medications, and others can inhibit renal tubular uptake, thus affecting drug clearance. Pharmacodynamic natural product–drug interactions are less well studied; however, additive, synergistic, or antagonistic effects have been observed. For example, the sedative effects of benzodiazepines are enhanced by concurrent valerian use, and the hepatotoxic effects of prolonged high acetaminophen doses may be increased with concomitant administration of comfrey.³¹ Because of the lack of quality published data, clinical pharmacists may find educating patients on natural product–drug interactions difficult.

Evaluation of Efficacy and Safety

When evaluating the efficacy and safety profile of an individual natural product to make patient care decisions, clinical pharmacists may initially consider using a straightforward benefit-risk method, as depicted in Figure 1.³² This method compares the current efficacy and safety of a natural product in four categories. Natural products with no efficacy and great risk should be avoided, or use discouraged, whereas those with great efficacy and low risk may potentially be

		← Efficacy →	
		High	Low
Safety	High	Evidence supports both safety and efficacy The natural product should fall within the standard of care and present limited risk to patients The clinical pharmacist may recommend the product but should continue to monitor its safety and efficacy	Evidence supports safety, but evidence regarding efficacy is inconclusive The natural product does not fall within the standard of care; however, it likely presents minimal risk to patients The clinical pharmacist may not specifically recommend taking this product; however, the pharmacist should urge caution and closely monitor it for efficacy
	Low	Evidence supports efficacy, but data regarding safety are inconclusive The natural product may potentially be viewed as a cause of patient injury; however, if the product presents a low risk of harm, it may be acceptable to use, depending on its level of efficacy The clinical pharmacist should consider tolerating a patient taking this natural product, urge caution, and closely monitor for safety	Evidence indicates serious risk or inefficacy The natural product is ineffective or may pose serious harm to the patient The clinical pharmacist should avoid recommending, and actively discourage patients from using, this natural product

Figure 1. Evaluation of the efficacy and safety risk of natural products. Adapted from.³²

recommended to the patient, depending on patient-specific factors.

Contemporary Natural Product Resources

Many online databases and websites are available for both patients and clinicians that provide evidence-based information on using natural products. Table 2 contains a list of databases and corresponding websites that provide information on natural products, including a description of the type of information provided, whether it is free or requires a subscription, whether it is referenced, and how often information is updated. In addition, print resources are available. However, online databases and websites are generally considered more current than print resources.

When recommending online resources to patients, clinical pharmacists should encourage patients to evaluate the quality of the information to ensure that it is current, accurate, and reliable. The National Library of Medicine has a tutorial on MedlinePlus that patients can use to evaluate the health information they find on the Internet. This may be a useful tool for clinical pharmacists to recommend to some patients.³³ In addition, when discussing online resources with patients who are interested in natural products, clinical pharmacists should caution individuals that some sites may be misleading and potentially dangerous. For example, patients should be wary of websites touting their products as “miraculous cures” or “breakthroughs” that can replace “dangerous prescription drugs” for chronic diseases. Terminology such as *detoxify* and similarly impressive-sounding words should raise concerns, as should statements that the product is “an ancient, all-natural remedy that pharmaceutical companies and the government have been suppressing.” Although some natural products may have efficacy, a clear risk of quackery also exists as companies promote potentially useless or even dangerous products.

Natural Products: Clinical Pharmacists and Patient Care

Patient-Centered Approach

Clinical pharmacists are medication use experts who are readily accessible members of the health care team. As a result, pharmacists are uniquely qualified and positioned to advise patients on the use of all medications, including natural

products.³⁴ The crucial first step in the clinical pharmacist’s patient care process is establishing the pharmacist-patient relationship, which allows open communication with the patient, family, and caregiver. Knowledge of patient experiences and expectations is fundamental to providing patient-centered care. The clinical pharmacist should understand the patient’s health care circumstances and preferences. Patients need to be comfortable discussing behaviors, concerns, preferences, health beliefs, and goals with their pharmacist, particularly with respect to natural product use. Clinical pharmacists can empower patients by providing them with the knowledge to make shared rational decisions. Involving patients in health care decisions will help them feel more involved and in control of their care.

Clinical pharmacists walk a fine line when discussing the use of natural products with patients. Many patients who actively use natural products do so secondary to strong beliefs that they are helping their current ailment, that the product is their only option because conventional therapy has failed, or that the product provides overall health promotion. However, some patients are hesitant to use such products because of their belief that these products are unorthodox and not part of traditional medicine or because of concerns regarding product efficacy or safety. Therefore, when discussing these products, clinical pharmacists should take a proactive, nonjudgmental approach and focus on shared decision-making between the patient, the pharmacist, and other health care providers. As part of this nonjudgmental method, pharmacists should avoid the use of product labels such as “alternative” and “complementary” when engaging patients in a discussion about natural products because patients may perceive these labels as biased toward “conventional” therapies.³⁵

A step-by-step approach is recommended that focuses on patient safety, extensive patient involvement in the decision-making process, and thorough documentation of the plan and associated goals.³⁶ The main goal of the discussion should be to help patients make informed decisions by providing them with objective information about the natural product. This information should include an assessment of the validity of the claims made about the natural product as well as the available evidence regarding its safety.³⁷ Open, respectful communication between the clinical pharmacist and the patient will develop trust and allow patients to be more

Table 2. Natural Product Resources

Database	Description	Free/Subscription	Updates
Health Care Professional Reference Databases Allied and Complementary Medicine Database (AMED)	<p>Publisher: British Library Health Care Information Service</p> <p>Content: A selection of about 600 journals in allied medical professions (occupational therapy, rehabilitation, physiotherapy, speech therapy, podiatry), complementary medicines, and palliative care</p> <p>Advantages: 152,000 records with 12,000 records added annually since 1985. All basic bibliographic information is included, with author abstracts, when available. Each record uses MeSH-controlled indexing terms for easy searches</p> <p>Disadvantages: Limited to mostly European sources. Although most articles are in English, many are not</p> <p>References: Database of primary literature articles URL: www.ovid.com/site/catalog/databases/12.jsp</p>	Subscription	Updated monthly
AMED-EBSCO	<p>Publisher: British Library Health Care Information Service</p> <p>Content: Alternative medicines database with information from 600 medical journals from 1995</p> <p>Advantages: Content from 600 journals dating back to 1995. All basic bibliographic information is included, with author abstracts when available</p> <p>Disadvantages: Limited to mostly European sources. Although most articles are in English, many are not</p> <p>References: Database of primary literature articles URL: https://www.ebscohost.com/academic/amed-the-allied-and-complementary-medicine-database</p>	Subscription	Updated monthly
American Botanical Council – HerbMedPro	<p>Publisher: American Botanical Council</p> <p>Content: Lists of botanical products with web links to information on evidence of efficacy in humans and web links to data from animal studies, analytical chemistry, pharmacokinetics and pharmacodynamics, and genetic studies. Links to safety, interactions, and contraindications are also provided. Links to color photos of the plants, to information on plant cultivation, and on botanical blends are available</p> <p>Advantages: Links to the original publications. The site is continuously updated and provides a brief history of the updates; some links have the full-text articles</p> <p>Disadvantages: The information is not summarized, so readers will need to go to the links provided. Subscription is required for full access to the botanical products</p> <p>References: The website provides links to additional content URL: http://cms.herbalgram.org/herbmedpro/overview.html?targetPage=http://cms.herbalgram.org/herbmedpro/index.html</p>	Subscription	Continuously updated
American Botanical Council – Expanded Commission E online	<p>Publisher: Integrative Medicine Communications</p> <p>Content: Monographs with information on description, chemistry/pharmacology, uses, contraindications, adverse effects, pregnancy/lactation, drug interactions, dosage/administration, and references</p> <p>Advantages: Monographs are generally concise. Some monographs available for free</p> <p>Disadvantages: The monographs do not appear to have been updated since 2000. They do not include the actual evidence supporting the botanical's use</p> <p>References: Yes URL: http://cms.herbalgram.org/expandedE/</p>	Subscription	Infrequent

(continued)

Table 2 (continued)

Database	Description	Free/Subscription	Updates
Cochrane Database of Systematic Reviews	<p>Publisher: Wiley Online Library</p> <p>Content: Systematic reviews of a natural product for a specific indication</p> <p>Advantages: Can use Boolean operators to refine searches. Summaries available in many languages. Full literature reviews are available. Access to summaries is free</p> <p>Disadvantages: Subscription required to view the full literature review. The reviews are not regularly updated</p> <p>References: Yes</p> <p>URL: www.cochrane.org/</p>	Subscription	Infrequent
Drugs.com MedFacts Natural Products Professional Database	<p>Publisher: Wolters Kluwer Health</p> <p>Content: Two ways to access content: (1) a brief overview and (2) a more comprehensive, evidence-based description of the following: uses, chemistry, dosing, contraindications, pregnancy/lactation, interactions, adverse reactions, and toxicology A detailed discussion of published reports on safety and efficacy is included. Some animal data are included</p> <p>Advantages: Natural products include botanical and non-botanical supplements, including other products such as Lorenzo's oil. Discussion of common as well as less well-known uses</p> <p>Disadvantages: Information is not updated regularly. Study descriptions of variable depth and not comprehensive. Distracting ads present on webpage</p> <p>References: Yes</p> <p>URL: www.drugs.com/npp/</p>	Free	Infrequent
Micromedex AltMedDex	<p>Publisher: Truven Health Analytics</p> <p>Content: Provides highlights of dosing, indications, contraindications, drug interactions, administration, and adverse effects for natural products</p> <p>Advantages: Collapsible sections allow user to go right to the section of interest. Links to "other sources"</p> <p>Disadvantages: Subscription required</p> <p>References: Yes</p> <p>URL: www.micromedexsolutions.com/micromedex2/4.24.0/WebHelp/Document_help/AltMedDex_Points.htm</p>	Subscription	Continuously updated
Natural Medicines	<p>Publisher: Therapeutic Research Center</p> <p>Content: Each monograph contains background, uses, safety, effectiveness, dosing, adverse effects, toxicology, drug interactions, mechanism of action, pharmacokinetics, summary evidence table, evidence discussion, and references</p> <p>Advantages: Lists of all potential uses as well as the dosing and efficacy for each specific use. 90,000 monographs are available in many languages and are updated yearly. Provides a proprietary rating of evidence. Each rating considers safety, efficacy, and product quality</p> <p>Disadvantages: Professional monographs are only available for specific ingredients within a product and not for products that contain multiple ingredients</p> <p>References: Yes</p> <p>URL: https://naturalmedicines.therapeuticresearch.com/</p>	Subscription	Yearly

(continued)

Table 2 (continued)

Database	Description	Free/Subscription	Updates
PubMed Dietary Supplement Subset	<p>Publisher: The National Center for Biotechnology Information</p> <p>Content: Full-text primary literature sources on dietary supplements in both humans and animals. Information includes chemistry, in vitro and in vivo biochemical function, clinical trials, and an overview of traditional Chinese and complementary medicine practices</p> <p>Advantages: Comprehensive coverage of supplements with a specialized search strategy to increase the efficiency of information gathering. Search-combination and filter tools allow for narrower searches</p> <p>Disadvantages: Not all content is available with free full text, and identified studies vary in their quality and relevance, making them time-consuming to search through, even with the specialized search strategy</p> <p>References: Database of primary literature articles URL: https://ods.od.nih.gov/Research/PubMed_Dietary_Supplement_Subset.aspx</p>	Free	Continuously updated
Review of Natural Products	<p>Publisher: Wolters Kluwer Health</p> <p>Content: Each monograph contains the scientific name of the product, common names, clinical overview, botany, history, chemistry, uses and pharmacology, dosing, pregnancy/lactation, interactions, adverse reactions, and toxicology. The clinical overview is a brief overview of natural products including uses, dosing, contraindications, pregnancy/lactation, interactions, adverse reactions, and toxicology</p> <p>Advantages: Detailed reviews of the top 440 natural products, with the top 300 continuously updated. Uses and pharmacology are divided into animal and human data. Natural products include botanical and non-botanical supplements, including other products such as Lorenzo's oil. Discussion of common as well as selected less well-known uses of natural products</p> <p>Disadvantages: Information on natural products outside the top 300 is not updated continuously and may not include newer studies</p> <p>References: Yes</p> <p>URL: http://online.factsandcomparisons.com/</p>	Subscription	Continuously updated
Reference Databases for Health Care Professionals and Patients ConsumerLab.com	<p>Publisher: ConsumerLab.com LLC</p> <p>Content: Independent product reviews, up-to-date information on warnings and recalls, a Natural and Alternative Treatments encyclopedia, and information on where to purchase the product. Site also includes a section where the website answers selected supplement questions from consumers</p> <p>Advantages: The supplement reviews consider many different brands and product manufacturers. Although written on a consumer level, the database is useful as well to a range of clinicians</p> <p>Disadvantages: Subscription is required for full access to the test results and to the discussion of products and recent studies</p> <p>References: Selected references are listed for the discussion of clinical uses and concerns</p> <p>URL: www.consumerlab.com/</p>	Subscription	Product reviews are updated periodically. Information on supplements updated as new studies are available

(continued)

Table 2 (continued)

Database	Description	Free/Subscription	Updates
MedlinePlus – Herbs and Supplements	<p>Publisher: National Library of Medicine (NLM)</p> <p>Content: Searchable database with links to websites or articles from the National Center for Complementary and Integrative Health, National Institutes of Health, Office of Dietary Supplements, and National Cancer Institute and reviews created by NLM, where patients and professionals can quickly find concise information. Contains information on efficacy, usual dose, and drug interactions</p> <p>Advantages: Easy-to-use database that provides information at an appropriate level of health literacy</p> <p>Disadvantages: The format and contents of articles vary by the organization providing the information</p> <p>References: Yes</p> <p>URL: https://www.nlm.nih.gov/medlineplus/druginfo/herb_All.html</p> <p>Publisher: Memorial Sloan Kettering Cancer Center</p> <p>Content: Searchable databases for health care professionals, patients, and caregivers.</p> <p>Concise descriptions of clinical evidence, uses, mechanisms of action, warnings, adverse reactions, and herb-drug and herb-lab interactions. Clinical summaries also mention uses outside oncology</p> <p>Advantages: Information for both health care professionals and patients is concise and understandable. Updated periodically by a pharmacist consulted by integrative medicine practitioners. Includes pictures of the parent plant</p> <p>Disadvantages: Information is not comprehensive or peer-reviewed, managed by a small team according to selected primary literature</p> <p>References: Yes</p> <p>URL: https://www.mskcc.org/cancer-care/treatments/symptom-management/integrative-medicine/herbs</p>	Free	Continuously updated
Memorial Sloan Kettering Cancer Center	<p>Publisher: National Cancer Institute</p> <p>Content: Information on natural products used for cancer treatment. Includes general summaries, laboratory studies, and clinical summaries of evidence</p> <p>Advantages: Easy-to-use and easy-to-access information for patients and health care professionals on products specifically used for cancer treatment. Primary literature sources are cited and easy to find</p> <p>Disadvantages: Key information such as dose, indication, and adverse effects not easy to find on their own; this information is included in block text. Includes information for only a few products</p> <p>References: Yes</p> <p>URL: www.cancer.gov/about-cancer/treatment/cam</p>	Free	Continuously updated
National Cancer Institute Complementary and Alternative Medicine	<p>Publisher: National Cancer Institute</p> <p>Content: Information on natural products used for cancer treatment. Includes general summaries, laboratory studies, and clinical summaries of evidence</p> <p>Advantages: Easy-to-use and easy-to-access information for patients and health care professionals on products specifically used for cancer treatment. Primary literature sources are cited and easy to find</p> <p>Disadvantages: Key information such as dose, indication, and adverse effects not easy to find on their own; this information is included in block text. Includes information for only a few products</p> <p>References: Yes</p> <p>URL: www.cancer.gov/about-cancer/treatment/cam</p>	Free	Continuously updated
Patient Reference Databases			

(continued)

Table 2 (continued)

Database	Description	Free/Subscription	Updates
Dietary Supplement Label Database	<p>Publisher: National Institutes of Health Office of Dietary Supplements</p> <p>Content: General information about the product, including serving information, dietary facts, label statements, and the manufacturer's contact information</p> <p>Advantages: All of the information on the product manufacturer's label is available</p> <p>Disadvantages: Not an all-inclusive list</p> <p>References: Yes</p> <p>URL: www.dsid.nlm.nih.gov/dsid/index.jsp</p>	Free	4 or 5 times/year
Mayo Clinic	<p>Publisher: Mayo Foundation for Medical Education and Research</p> <p>Content: Background information, dosing, evidence summaries, dosing, safety concerns, interactions, methodology, and references for a selected number of common natural products</p> <p>Advantages: Assigns easy-to-read "grade" for clinical evidence for each indication</p> <p>Disadvantages: Not a comprehensive source. Information limited to high-use agents. Consumers may have problems reading and understanding some sections</p> <p>References: Yes</p> <p>URL: www.mayoclinic.org/drugs-supplements</p>	Free	Frequent
National Cancer Institute – Office of Cancer Complementary and Alternative Medicine	<p>Publisher: National Institutes of Health</p> <p>Content: Health information for patients and professionals on complementary and alternative medicines used in cancer treatment from the National Center for Complementary and Integrative Health, National Cancer Institute, and Office of Cancer Complementary and Alternative Medicine. Also contains research results, overviews of natural product use, and a list of current clinical trials involving natural products</p> <p>Advantages: Includes therapies that are not herbal or supplemental products, such as acupuncture and exercise</p> <p>Disadvantages: Some topics are vague, and many topics overlap with each other</p> <p>References: No</p> <p>URL: http://cam.cancer.gov/health_information/cam_therapies_a-z.htm</p>	Free	Infrequent
National Center for Complementary and Integrative Health	<p>Publisher: National Center for Complementary and Integrative Health</p> <p>Content: Fact sheets for herbs and botanicals with information on common names, scientific name, evidence for use, potential adverse effects and cautions, and resources for more information</p> <p>Advantages: Easy-to-use format that allows a user to quickly access a particular agent, or the entire site can be downloaded as a booklet. Includes pictures of the botanical</p> <p>Disadvantages: Infrequently updated. There is a mixture of source quality, depending on agent</p> <p>References: Yes</p> <p>URL: https://nccih.nih.gov/health/herbsataglance.htm</p>	Free	Infrequent
National Institutes of Health Office of Dietary Supplements	<p>Publisher: National Institutes of Health</p> <p>Content: Fact sheets from the National Center for Complementary and Integrative Health and the National Institute of Environmental Health Sciences on selected products. Contains links to learn more about the product</p> <p>Advantages: Most fact sheets have links to monograph and toxicology information. Easy to read and understand for patients</p> <p>Disadvantages: Is not regularly updated</p> <p>References: Yes</p> <p>URL: https://ods.od.nih.gov/factsheets/list-all/</p>	Free	Infrequent

(continued)

Table 2 (continued)

Database	Description	Free/Subscription	Updates
RxList.com – Vitamins, Herbs, and Dietary Supplements	<p>Publisher: RxList Incorporated Content: Monographs contain indications and evidence for use, how the drug works, safety concerns, drug interactions, and dosing considerations Advantages: Comprehensive list of agents. Quick links help jump faster to the desired information for each agent Disadvantages: Many distracting ads on the webpage, which is updated irregularly References: No URL: www.rxlist.com/supplements/article.htm</p>	Free	Infrequent
University of Maryland Medical Center: Complementary and Alternative Medicine Guide	<p>Publisher: University of Maryland Medical Center Content: Each natural agent has information on uses, a description of the plant, dosage forms, precautions, interactions, and references Advantages: Many ways to search for information – disease state, symptoms, agent, adverse effect, warning, and interactions Disadvantages: Drug information is incomplete; dosages, frequencies, and durations not listed References: Yes URL: http://ummm.edu/health/medical/altmed</p>	Free	Infrequent

willing to discuss their use of or lack of desire to use, natural products. Regardless of the patient's decision with respect to natural products, it is imperative that the clinical pharmacist keep timely documentation of the medication therapy plan and continue to be supportive of the patient.

Patient Assessment

The ACCP Standards of Practice for Clinical Pharmacists provide a framework for delivering comprehensive medication management and related care that can be applied to the natural product arena.³⁸ The standards recommend that the clinical pharmacist assess the patient's medication-related needs by:

- Reviewing the medical record using a problem-oriented framework (e.g., interpreting and analyzing subjective and objective information) to determine the patient's clinical status;
- Meeting with the patient/caregivers to obtain and document a complete history to identify all of the patient's current medications (including regimens and administration routes for any prescription or nonprescription drugs, vaccines, or natural products), medication-taking behaviors, adherence, allergies, and attitudes and experiences with therapies;
- Obtaining, organizing, and interpreting patient data; and
- Prioritizing patient problems and medication-related needs.

For patients using natural products, clinical pharmacists should determine the appropriateness and safety of the product and ascertain whether conventional medication or another natural product would be more appropriate. Clinical pharmacists should also review the patient's drug regimen and disease states to eliminate product duplications or products that do not provide therapeutic benefit. Moreover, they should caution against using natural products when assessing patients who are pregnant, immunosuppressed, or being treated for cancer. Allergies must be carefully reviewed because many natural products produce cross-reactivity to other natural products (e.g., similar plant species, pollen).¹

Patient Education

Clinical pharmacists delivering direct patient care are well positioned to integrate a consistent

process of care for patients taking natural products. Available data indicate that pharmacists are more objectively knowledgeable about natural products relative to other clinicians and health food store representatives.^{39, 40} However, pharmacists' self-perceived preparedness and basic knowledge about natural products remains low, despite regular questions from patients. This deficiency is exacerbated by a poorly defined role, barriers to effective communication, and missed opportunities for patient engagement and education.^{41, 42}

Initiating the conversation about natural products with patients can be challenging for clinical pharmacists. Eisenberg suggests that all clinicians begin conversations about natural products by connecting the use of a natural product with a patient's chief concern.³⁶ Skillfulness in this approach requires pharmacists to have adequate general knowledge about natural products so that targeted questions can ease patients into a difficult conversation. An example of a targeted question would be: "Some people have used saw palmetto for problems urinating. Have you used or thought about using a natural product for symptom relief?" Although many patients use natural products complementary to conventional therapies (vs alternative to conventional therapies), there is still concern that patients may self-treat in place of seeking out medical care.^{34, 35} Clinical pharmacists in a community setting, in particular, where natural products are often sold, have the unique opportunity to affect patient care at the point of sale, which may hasten assessment or referral for a patient's unmet medical need.

Similar to how clinical pharmacists first engage in a discussion about natural products, the information collected merits consideration and tact. Recognizing also that pharmacists often have significant time constraints, the data collected must be prioritized to maximize patient safety. If patients are taking natural products for a specific indication, this should be clarified during the discussion. Ideally, after the principal symptom is identified, patients should be educated on how to track progress using a symptom diary. Within this diary, patients should keep a daily and objective record of natural product use, especially when reported safety and efficacy data are sparse.^{35, 36} Other important considerations are patient preferences and expectations (i.e., symptom relief vs curative properties) for natural products.

At every opportunity, clinical pharmacists should discuss the risks, benefits, and

cost-effectiveness of natural products in the context of evidence-based therapies and applicable alternatives. Patients using natural products for general health improvement (i.e., not for a specific indication) must also be educated on the pertinent risks and costs. In addition, even when safety and efficacy are well defined for a particular natural product, variability in manufacturing creates opportunities to educate patients on the risk of adulterated and misbranded products (e.g., impurities or products containing FDA-banned substances).

Patients stabilized on a combination regimen of a natural product with any conventional medication (nonprescription or prescription) should be informed not to suddenly discontinue the use of either without consulting their prescriber or pharmacist. The potential for adverse events from a drug interaction may result when a natural product is discontinued or initiated.³⁴ An adverse event may also occur when the dose of either product is changed without consulting the prescriber. Given the widespread and indiscriminate use of natural products, pharmacists have a professional obligation to detect and prevent drug interactions and adverse events between natural products and conventional medication.

Monitoring and Follow-up

The clinical pharmacist should also monitor and evaluate the effectiveness of the care plan involving the natural product. The clinical pharmacist's patient care process includes continuous monitoring and evaluation for appropriateness, effectiveness, safety, patient adherence, and patient feedback.⁴³ Clinical end points should be established that contribute to the patient's overall health. In a recent survey, Canadian stakeholders, including consumer groups, conventional and alternative medicine practitioners, and natural product industry groups and pharmacy leaders, expressed a consensus that it is the pharmacist's responsibility to monitor the safety of natural products.⁴⁴ This survey was small, but it reinforces the pharmacist's important role in therapy monitoring. Unfortunately, ensuring the safety and efficacy of natural products is difficult, given the paucity of reliable and reproducible data on natural products. Outcomes of care, including how the patient is progressing toward, or has achieved, the goals of natural product therapy, must be evaluated. When enough data are available, clinical pharmacists should also share this information,

including monitoring strategies, timelines for intended or unintended outcomes, and patient satisfaction.

Care Transitions/Discharge Planning

The clinician's acknowledgment of natural product use should not end after an accurate medication history has been obtained but should be integrated into the patient's individualized treatment plan. The clinical pharmacist should complete a thorough evaluation of natural products to optimize medication therapy and reduce the possibility of natural product–drug interactions and natural product–disease interactions.^{38, 45} A patient-centered approach is vital during all points of transition of care. The clinical pharmacist should evaluate each natural product to determine whether it is clinically appropriate to continue, suspend, or discontinue. If natural products are unfamiliar, a literature review of the patient's medications and possible interactions should be completed. All products should be evaluated for their evidence of benefit or harm, cost, and appropriateness, depending on the patient's clinical condition.³⁸ If natural products are deemed to be suspended or discontinued because of lack of evidence supporting their use during hospitalization, it is important to develop a plan to taper or discontinue them, depending on their pharmacologic properties. For example, if a patient has been using exogenous hormones, it may be necessary to complete a testosterone taper with repeated laboratory tests. It is important to ensure that an open dialogue exists between health care providers and the patient that is neither negative nor dismissive.

The discharge process is a crucial step to ensure that the patient and all members of the health care team are in agreement with the medication regimen, including natural products, on discharge. The clinical pharmacist should openly and effectively communicate with patients and their outside health care providers regarding the optimized treatment plan. The plan should include the medications and/or natural products being discontinued at discharge and the medications and/or natural products being added. More specific discussion should describe the indication of the medications and/or natural products, goal of the therapeutic regimen, and possible adverse reactions.³⁷ If, at the time of discharge, it is decided to discontinue a natural product, the clinical pharmacist and patient should discuss the reasoning, including the available

efficacy and safety evidence, for no longer using the product. Likewise, if a natural product is initiated, the patient should be educated on product selection (i.e., a USP- or NSF-certified product), dosing, administration, and adverse effects, and patient follow-up and monitoring should be coordinated with outside providers. Clinical pharmacists should document the addition of this natural product to the medication plan of care in the medical record, and a copy should be provided to the patient and the patient's outside providers, including pharmacies. Documentation should include the specific medication therapy plan (e.g., dose, route, frequency, and relevant monitoring parameters), a detailed synopsis of the education provided to the patient regarding the medication therapy plan, and a collaborative plan for evaluating and monitoring the new regimen, including follow-up and future visits.³⁸

Summary

Natural products are widely used by patients, despite limited high-quality efficacy and safety data to support their use. Clinical pharmacists can play a key role in educating patients on efficacy and safety concerns, availability of natural product references, and regulatory issues. Because of their accessibility, clinical pharmacists can also form a strong patient relationship that provides a framework for the delivery of comprehensive medication management for natural products. This approach will allow the clinical pharmacist to assess patients, ensure smooth care transitions, and strengthen collaboration among clinicians regarding the appropriate use of natural products.

References

1. Miller LG, Hume A, Harris IM, et al. White paper on herbal products. *American College of Clinical Pharmacy. Pharmacotherapy* 2000;20:877–91.
2. National Center for Complementary and Integrative Health (NCCIH). Natural products research – information for researchers. Available from https://nccih.nih.gov/grants/natural_products. Updated June 7, 2016. Accessed August 23, 2016.
3. U.S. Food and Drug Administration (FDA). What is a dietary supplement? Available from www.fda.gov/AboutFDA/Transparency/Basics/ucm195635.htm. Updated June 8, 2015. Accessed May 23, 2016.
4. Global Industry Analysts, Inc. The global herbal supplements and remedies market: trends, drivers and projections, February 2015. Available from www.strategyr.com/MarketResearch/Herbal_Supplements_and_Remedies_Market_Trends.asp. Accessed May 23, 2016.
5. Smith T, Lynch ME, Johnson J, Kawa K, Bauman H, Blumenthal M. Herbal dietary supplement sales in US increase 6.8% in 2014. *HerbalGram* 2015;107:52–9.

6. Wu CH, Wang CC, Tsai MT, Huang WT, Kennedy J. Trend and pattern of herb and supplement use in the United States: results from the 2002, 2007, and 2012 National Health Interview Surveys. *Evid Based Complement Alternat Med* 2014;2014:872320.
7. Gardiner P, Graham R, Legedza AT, Ahn AC, Eisenberg DM, Phillips RS. Factors associated with herbal therapy used by adults in the United States. *Altern Ther Health Med* 2007;13:22–9.
8. Horrigan B, Lewis S, Abrams D, Pechura C. Integrative medicine in America: how integrative medicine is being practiced in clinical centers across the United States. *Glob Adv Health Med* 2012;1:18–94.
9. U.S. Food and Drug Administration (FDA). Dietary supplements. Available from www.fda.gov/Food/DietarySupplements/. Updated April 4, 2016. Accessed July 1, 2016.
10. Swann JP. The history of efforts to regulate dietary supplements in the USA. *Drug Test Anal* 2016;8:271–82.
11. U.S. Food and Drug Administration (FDA). FDA 101: dietary supplements. Available from www.fda.gov/ForConsumers/ConsumerUpdates/ucm050803.htm#HowAreSupplementsRegulated. Updated July 25, 2015. Accessed May 23, 2016.
12. Federal Trade Commission (FTC). Dietary supplements: an advertising guide for industry. Available from <https://www.ftc.gov/tips-advice/business-center/guidance/dietary-supplements-advertising-guide-industry>. Accessed July 1, 2016.
13. U.S. Food and Drug Administration (FDA). Dietary supplement current good manufacturing practices (CGMPs) and interim final rule (IFR) facts. Available from www.fda.gov/Food/GuidanceRegulation/CGMP/ucm110858.htm. Updated September 19, 2014. Accessed July 1, 2016.
14. United States Pharmacopeia (USP). USP verified dietary supplements. Available from www.usp.org/usp-verification-services/usp-verified-dietary-supplements. Accessed May 23, 2016.
15. National Sanitation Foundation (NSF). Dietary supplement safety. Available from www.nsf.org/services/by-industry/dietary-supplements/supplement-safety. Accessed May 23, 2016.
16. Srinivascan VS, Provar LN. USP verified dietary supplements. In: Bonakdar RA, ed. *The H.E.R.B.A.L. guide: dietary supplement resources for clinicians*. New York, NY: Lippincott Williams & Wilkins, 2012:122–25.
17. California Department of Public Health (CDPH). Dietary supplement manufacturers. Available from <https://www.cdph.ca.gov/programs/pages/fdbdietarysupplements.aspx>. Updated January 29, 2015. Accessed July 1, 2016.
18. Centre for Evidence-Based Medicine (CEBM). Oxford Centre for Evidence-Based Medicine levels of evidence (March 2009). Available from www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/. Accessed August 23, 2016.
19. National Center for Complementary and Integrative Health (NCCIH). Use of complementary health approaches in the U.S. National Health Interview Survey (NHIS). Most used natural products. Available from <https://nccih.nih.gov/research/statistics/NHIS/2012/natural-products>. Updated December 2, 2015. Accessed June 19, 2016.
20. Wolsko PM, Solondz DK, Phillips RS, Schachter SC, Eisenberg DM. Lack of herbal supplement characterization in published randomized controlled trials. *Am J Med* 2005;118:1087–93.
21. Linde K, Berner MM, Kriston L. St John's wort for major depression. *Cochrane Database Syst Rev* 2009;4:CD000448.
22. Gagnier JJ, Boon H, Rochon P, Moher D, Barnes J, Bombardier C, CONSORT Group. Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. *Ann Intern Med* 2006;144:364–7.
23. Newmaster SG, Grguric M, Shanmughanandhan D, et al. DNA barcoding detects contamination and substitution in North American herbal products. *BMC Med* 2013;11:222.
24. Gardiner P, Sarma DN, Low Dog T, et al. The state of dietary supplement adverse event reporting in the United States. *Pharmacoepidemiol Drug Saf* 2008;17:962–70.
25. Felix TM, Karpa KD, Lewis PR. Adverse effects of common drugs: dietary supplements. *FP Essent* 2015;436:31–40.
26. Geller AI, Shehab N, Weidle NJ, et al. Emergency department visits for adverse events related to dietary supplements. *N Engl J Med* 2015;373:1531–40.
27. Stickel F, Shouval D. Hepatotoxicity of herbal and dietary supplements: an update. *Arch Toxicol* 2015;89:851–65.
28. Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. *Gastroenterology* 2015;148:517–32.e3.
29. Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther* 2013;37:3–17.
30. Posadzki P, Watson L, Ernst E. Herb-drug interactions: an overview of systematic reviews. *Br J Clin Pharmacol* 2013;75:603–18.
31. Alissa EM. Medicinal herbs and therapeutic drug interactions. *Ther Drug Monit* 2014;36:413–22.
32. Cohen MH, Eisenberg DM. Potential physician malpractice liability associated with complementary and integrative medical therapies. *Ann Intern Med* 2002;136:596–603.
33. U.S. National Library of Medicine (NLM). Evaluating internet health information: a tutorial from the National Library of Medicine. Available from www.nlm.nih.gov/medlineplus/webeval/webeval.html. Updated May 2, 2016. Accessed May 24, 2016.
34. Kroll DJ. ASHP statement on the use of dietary supplements. *Am J Health Syst Pharm* 2004;61:1707–11.
35. Perlman AI, Eisenberg DM, Panush RS. Talking with patients about alternative and complementary medicine. *Rheum Dis Clin North Am* 1999;25:815–22.
36. Eisenberg DM. Advising patients who seek alternative medical therapies. *Ann Intern Med* 1997;127:61–9.
37. Smith M, Boon HS. Counseling cancer patients about herbal medicine. *Patient Educ Couns* 1999;38:109–20.
38. American College of Clinical Pharmacy (ACCP). Standards of practice for clinical pharmacists. *Pharmacotherapy* 2014;34:794–7.
39. Kemper KJ, Gardiner P, Gobble J, Woods C. Expertise about herbs and dietary supplements among diverse health professionals. *BMC Complement Altern Med* 2006;6:15.
40. Coon SA, Stevens VW, Brown JE, Wolff SE, Wrobel MJ. Comparison of dietary supplement product knowledge and confidence between pharmacists and health food store employees. *J Am Pharm Assoc* 2015;55:161–8.
41. Brown CM, Pena A, Resendiz K. Pharmacists' actions when patients use complementary and alternative medicine with medications: a look at Texas-Mexico border cities. *J Am Pharm Assoc* 2011;51:619–22.
42. Kwan D, Hirschhorn K, Boon H. U.S. and Canadian pharmacists' attitudes, knowledge, and professional practice behaviors toward dietary supplements: a systematic review. *BMC Complement Altern Med* 2006;6:31.
43. Joint Commission of Pharmacy Practitioners (JCPP). Pharmacists' patient care process. May 29, 2014. Available from www.pharmacist.com/sites/default/files/files/PatientCareProcess.pdf. Accessed October 21, 2016.
44. Olatunde S, Boon H, Hirschhorn K, Welsh S, Bajcar J. Roles and responsibilities of pharmacists with respect to natural health products: key informant interviews. *Res Social Adm Pharm* 2010;6:63–9.
45. Klepser TB, Doucette WR, Horton MR, et al. Assessment of patients' perceptions and beliefs regarding herbal therapies. *Pharmacotherapy* 2000;20:83–7.