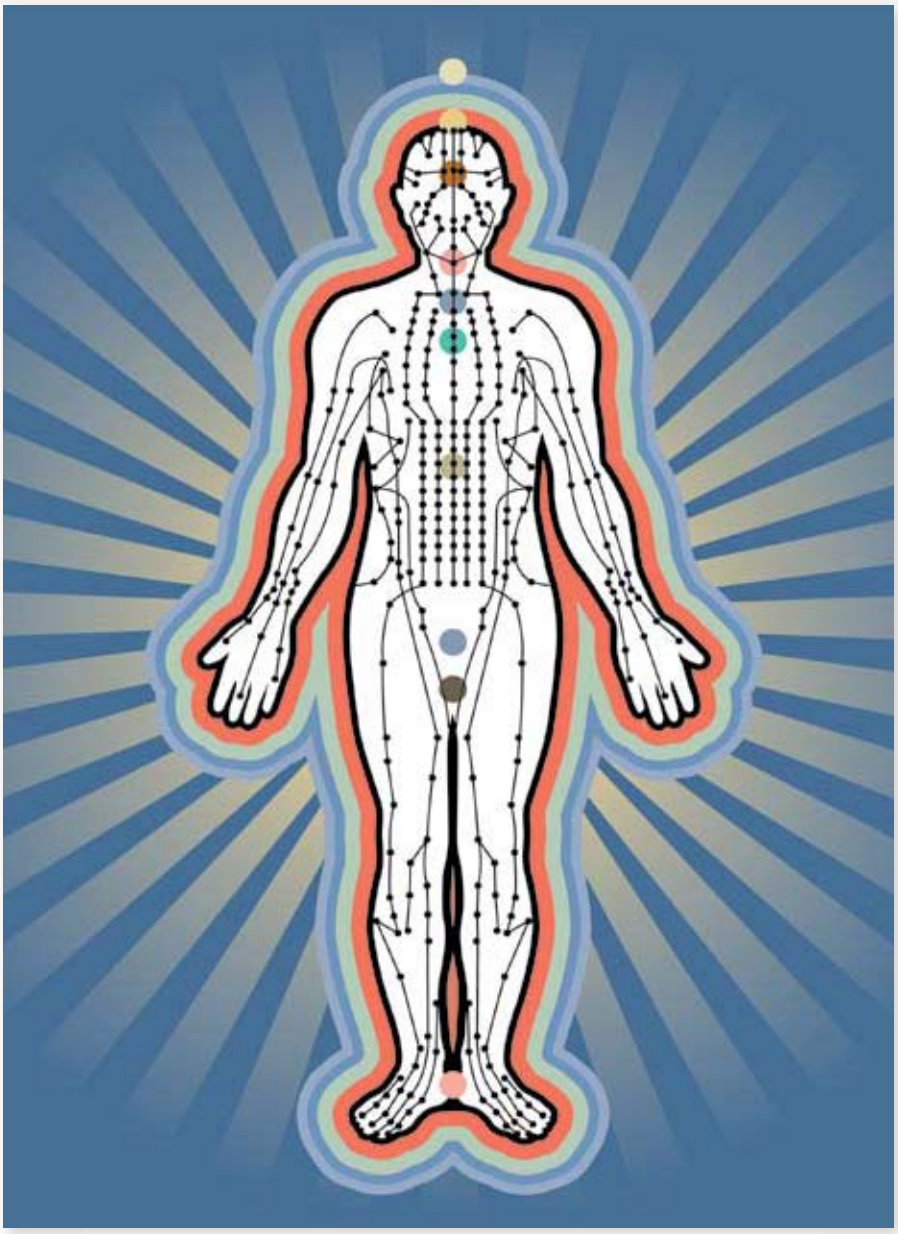
Introduction to Naturopathic Medicine

by Shannon Sinsheimer, N.D.



I would first like to thank the California Pharmacist's Association for the opportunity to contribute to this publication. I am ecstatic to assist in facilitating a more comprehensive understanding of the practice, education, and laws pertaining to naturopathic medicine. Through this edition I hope the reader will extract applicable information to use in practice, a working knowledge of the prescription rights of naturopathic doctors, and a basic understanding of the foundations of naturopathic medicine so that we may continue to foster a productive integrative environment.

Naturopathic medicine, summarized, is the application of a holistic medical philosophy that strives to treat the underlying cause of disease while eliminating obstacles to health. It is a focus on stimulating the body's inherent ability to heal using primary natural remedies. Based on this philosophy many Naturopathic Doctors (NDs) do not routinely prescribe pharmaceutical medications. This is in part due to the fact that a large portion of our patient base is seeking treatment for chronic illness, which, does not warrant acute prescription care. It is also because we have a host of remedies that can effectively replace certain pharmaceutical medications. Although the majority of NDs do not utilize pharmaceuticals as part of their regularly regime there is still an inherent respect and gratitude for the role pharmaceuticals and Pharmacists play in mainstream and natural healthcare. And because many NDs do not regularly prescribe pharmaceuticals, we are even more grateful when we have our local Pharmacist to turn to when we need advice on prescription choices.

My opinion is one of many, but I enjoy the integrative community created by accessing one another's expertise for the optimization of healthcare for our patients. Through ongoing communication and co-education between our specialties we can learn what the most effective protocols for the specific needs of each patient are. Wellness plans that include a variety of information from each specialist take into account various perspectives and create a larger array of options.

As I appreciate the advice and recommendations of my local Pharmacist, please do not hesitate to call upon the education and advice of your local ND. If there is a question regarding herbal/supplement-drug interaction, mechanism of action of a natural remedy, or a new natural therapy your patient or customer is using, an ND will be more than happy to share their knowledge on the subject with you.

I look forward to the continued relationship between Pharmacists and Naturopathic Doctors and I hope you find the information in this edition of your publication useful.

A Naturopathic Doctor's Scope of Practice Related to Pharmaceuticals

by Peter Wanningman, N.D., R.Ph.

Naturopathic Doctors, Prescribing, Pharmacy, California.

Although commonly unfamiliar to most long time residents of California, naturopathic medicine is an enterprising expansion of what is seen as the traditional allopathic model of medicine. With the passage of the Naturopathic Doctors Act of 2004 (the Act), naturopathic doctors became licensed to diagnose and treat in the State of California. It is a profession overseen by the Bureau of Naturopathic Medicine (the Bureau) which is within the Department of Consumer Affairs. This Act outlined the practice guidelines for naturopathic doctors (NDs), similar to other practitioners in the State of California, including but not limited to medical doctors, nurse practitioners, physician assistants, and, of course, pharmacists. One common thread between all these aforementioned practitioners is the right to prescribe prescription medications in California.

The following article will attempt to shed some light on this new profession to California. This is especially important knowledge to acquire for the pharmacist, since it is the pharmacist that ultimately acts as the gate keeper in prescribing. Appropriately then, the article will briefly describe the philosophy and history of the profession, including the legislative history in California. It will also offer insight into the rational for ND prescribing, delineate the current scope of practice and prescribing, as well as provide links to valuable resources for expanded information on naturopathic medicine.

Brief History of Naturopathic Medicine

The roots to naturopathic medicine find it as one of the oldest continuously licensed health care professions in the country. Dr. Benedict Lust is commonly considered the "Father" of naturopathic medicine. Other founding influences on naturopathic medicine include mid-19th century German founder of hydrotherapy, Sebastian Kneipp and father of homeopathy, Dr. Samuel Hahnemann.

The first organized school for the profession was Lust's American School of Naturopathy in New York, opening in 1901. The school groomed physicians utilizing principles based on nutrition, exercise, detoxification, botanical (plant) medicine, homeopathy, and physical medicine. The profession found itself gaining huge popularity and the number of schools burgeoned to more than a dozen by 1925. Regulation of the schools and profession within individual states created a platform for the standard allopathic wing of medicine to oppose naturopathic medicine.

The hey-day of allopathic medicine reached a pinnacle standard in the post World War II era with the advent of antibiotic therapy. This set the way for a much more defined model of allopathic medicine and a pharmaceutical-based paradigm of treatment. During this same time, naturopathic medicine saw a loss of popularity, until a renewed interest developed again in the 1970's.

Today, there are 13 states which license naturopathic doctors. California became a licensed state in 2004. There are prominent licensing acts in process in 15 states, including probable legislation in an additional eight states, including New York.

The modern-day philosophy of naturopathic medicine is firmly grounded into six principles:

1. Identify and Treat the Cause - Utilizing the symptoms as an avenue to identify the cause and then develop a treatment plan focused on modulating the causers.
2. The Healing Power of Nature- Understanding the healing power of nature and the inherent ability of the human body to heal itself, when the obstacles to cure are removed.
3. First Do No Harm - This delivers the practitioners intent to utilize modalities and treatments that minimize the affect on the vital, living system while utilizing minimal force and attempting to avoid suppressive choices when appropriately assessed.
4. Treat the Whole Person - The ND considers disease as a dis-ease to the person. This disturbance to the person can be evaluated as a multifactorial picture that includes the physical, mental and spiritual well-being as integral pieces to the whole person.
5. Prevention - Putting forth treatment plans to allow for less opportunity for the disorder to happen or recur.
6. Doctor as Teacher - Patient education. NDs spend time with their patients, helping to teach them, so that they learn and understand the basis to their illness.

Education and Training

Naturopathic doctors attend medical universities that are accredited by the Council on Naturopathic Medical Education (CNME). There are currently six accredited schools in North America which have met this approval process.

The NDs four-year post graduate education is very similar in format to that of allopathic, and osteopathic medical schools, in which the first two years have an emphasis on the basic sciences, followed by core clinical sciences in the last two years. Specifically, the pharmacology education is based on components of pharmacodynamics and pharmacokinetics as well as clinical applications of drug utilization. The didactic requirement for obtaining a furnishing license in the State of California is 48 hours of pharmacology, yet most schools are

either currently offering or developing coursework to accommodate at least 110 hours of pharmacology.

In order to become licensed, NDs must complete and pass examinations offered by the North American Board of Naturopathic Examiners. There are two parts to the exam. Part I is offered after the completion of basic science requirements (2nd year) in school and successful passage is a requirement before being able to sit for Part II. The Part I exam tests knowledge on:

- Physiology
- Pathology
- Anatomy
- Biochemistry
- Microbiology

The Part II exam is offered after graduation (4th year). It is a comprehensive clinical examination utilizing case studies and general stand-alone questions covering nine different clinical areas of study:

- Pharmacology
- Botanical Medicine
- Physical and Clinical Diagnosis
- Lab Diagnosis and Imaging
- Nutrition
- Psychology
- Physical Medicine
- Emergency Medicine
- Homeopathy

The State of California requirements for an ND license maintains that the ND must successfully graduate from an accredited school, pass the board exams, as well as many other criteria. A furnishing license is optional to the ND, but is required if he/she chooses to furnish dangerous drugs.

Once licensed, the ND must complete 60 hours of approved continuing education, of which no less than 20 hours must be in pharmacotherapeutics.

Naturopathic Doctors, Dangerous Drugs and the Rational for Prescribing

Under the pretense of the principals or code by which NDs operate, it can be confusing to understand the philosophy which the ND uses to consider pharmaceutical agents in a treatment program. Keeping in mind that the ND is seen by a patient to be a primary care practitioner, it is reasonable to assume a wide array of treatment plans needs to be considered when approaching the patient.

It should be understood, that under general circumstances, inherently NDs will not use prescription medications in first-line treatment plans. Rather, the therapeutic hierarchy which drives the philosophy of an ND will initiate with a focus on stimulating the natural, self-healing capacity of the system. They will take into consideration the insufficiency of organ systems, followed by considering the integral structural integrity of the system. When the evaluation and treatment plan goes deeper, the disordered pathology is addressed by the use of well-prescribed natural substances, modalities and techniques. In the last steps of the hierarchy, the ND will orchestrate the use of synthetic, pharmaceutical substances, which may indeed act to suppress the pathology of the system.

Take for example a patient who presents with acute pharyngitis and tests positive for Group A-Strep. Antibiotic therapy is a standard of care for **both** allopathic and naturopathic models, only in the ND model, a naturopathic treatment plan would typically be initiated as the first-line if intervention. Depending on the presentation of the patient, an example of a well thought out naturopathic protocol might look like the following:

- Use of a combination botanical formula, with herbs such as oregano, echinacea,

Homeopathy: A well-selected homeopathic remedy, prescribed on the presentation of the acute picture of the patient.

andrographis, garlic, and elderberry which act with immune modulating capacities to allow the natural immunity to facilitate an up-regulated action on the infection.

- Hydrotherapy: The act of using properties of water to facilitate the movement of lymph and blood, creating a more vital flow of fluids in contrast to the congestion presented during an illness.
- Homeopathy: A well-selected homeopathic remedy, prescribed on the presentation of the acute picture of the patient. Acute remedies are dosed frequently and typically a new prescription is generated when the symptom picture changes. Common remedies that may be found to be useful in this type of presentation may include but are not limited to: belladona, phosphorus, causticum, argentum metallicum, aconite and sulphur.
- Conscientious follow up within a window of hours would identify the need and justification to move through the hierarchy of treatment considerations and ultimately, if the presentation did not respond favorably to the ideal treatment approach, then appropriate antibiotic therapy would safely and appropriately commence. It should be duly noted, that responsible diagnosis and treatment may justify that the ND initiate antibiotic therapy on the first step treatment hierarchy, naturally dependent on the state of presentation of the patient and the patient's informed consent of the treatment options available to them.

Another, yet different understanding for the rational behind prescribing could involve a patient who presents to a ND after seeing an allopathic practitioner whom has the patient already on one or more prescription medications. Take for instance a Type II diabetic with out of range blood glucose when the patient's drug therapy includes maximum recommended doses of metformin. When this patient presents to the ND, as the primary care practitioner, the ND would likely follow the hierarchy of treatment. After a period of time, it may become evident that the naturopathic treatment has successfully assisted the patient in lowering the blood glucose levels and would justify a lowering of the metformin dose. It is necessary for the ND to be a licensed prescriber in order to facilitate the ordering of this new lower dose of metformin. Without proper licensing authority, the ND would need to send the patient to another class of practitioner simply to adjust the dose of the patient's medication regimen. This would create unnecessary medical costs to the patient, and perhaps, even burden the patient with unwarranted invention by a practitioner within a paradigm of medicine that the patient may have chosen to avoid in the first place, preferring instead, the naturopathic practitioner for their alternative, drug-minimizing philosophy of medicine.

Naturopathic Drug Formulary

The Naturopathic Doctors Act of 2004 (Section 3640(c)) authorized ND to dispense, administer, order and prescribe:

1. Food, extracts of food, nutraceuticals, vitamins, amino acids,minerals, enzymes, botanicals and their extracts, botanical medicines, homeopathic medicines, all dietary supplements and nonprescription drugs as defined by the federal Food, Drug, and Cosmetic Act, consistent with the routes of administration identified in subdivision (d).
   d) A naturopathic doctor may utilize routes of administration that include oral, nasal, auricular, ocular, rectal, vaginal, transdermal, intradermal, subcutaneous, intravenous, and intramuscular. (it is further regulated by the Bureau of Naturopathic Medicine (Title 16 C.C.R section 4323(d)) that an ND may utilize the IV and and ocular routes of administration only if the ND is clinically competent in those areas).

In Section 3640.7, the Act authorizes NDs to independently prescribe epinephrine to treat anaphylaxis and natural and synthetic hormones. Any other prescribing outside the perimeters of this independent prescribing is authorized if done under the supervision of a medical doctor. Section 3640.5 identifies the requirements for the standardized procedures and protocols related to this supervised prescribing, which are essentially the same as nurse practitioners (sans the requirements for diagnosing and treating). This Act does make inclusion for the furnishing and ordering of Schedule III-V controlled substances, provided the ND holds a current DEA license.

In summary, an ND may:

- Independently **prescribe**:
  - Hormones, synthetic or natural, including CIII testosterone
  - Epinephrine in the treatment of anaphylaxis
- **Order or Furnish** under MD supervision:
  - Dangerous drugs
    - as defined by the collaborative procedures and protocols established between the ND and MD.
  - Schedule III-V controlled substances

Restrictions to a NDs practice are identified by Section 3642 of the Act. They include:

- Administering therapeutic ionizing radiation or radioactive substanc
- Administering spinal anesthesia
- Performing abortions
- Performing any surgical procedure

The exact language can be found online at http://www.naturopathic.ca.gov/laws/index.shtml, with special attention paid to section 3640.

The Act also called for the Bureau to establish a Naturopathic Formulary Advisory Committee to review naturopathic education, training and practice and make specific recommendations regarding the prescribing, ordering, and furnishing authority of a naturopathic doctor and the required supervision and protocols for those functions. The committee would also determine the naturopathic formulary of dangerous drugs.

The committee was composed of an equal number of naturopathic doctors, medical doctors and pharmacists. Each profession was represented from the clinical and academic settings and helped in developing findings and recommendations of ND prescribing and practice. After 15 meetings over 16 months, the committee developed

recommendations and findings that were ultimately presented to "and accepted by the Department of Consumer Affairs in January 2007" and subsequently "signed off by the Governor's office as a first step towards writing legislation to correct the current paradigm."

The report found that the 13 states, other than California, that license naturopathic doctors, only one required MD supervision, with that being the state of Kansas, which makes up only 0.5% of licensed NDs nationwide. While each state does have a formulary, they vary greatly. Arizona has the broadest formulary, as well as a post-graduate 60 hour pharmacy course and examination requirement for NDs. Arizona NDs can independently prescribe all dangerous drugs, except:

- Controlled substances CI and CII
- Antipsychotics
- Cancer chemotherapeutic drugs
- IV drugs (omitting IV vitamins, drugs used in chelation, and drugs used for emergency resuscitation and stabilization)

The committee also found that as a whole, NDs were highly safe prescribers. They found that there were no reports of harm or disciplinary actions by any state board against any ND for prescribing. When studied further, the committee inquired with one of the largest malpractice insurers of NDs about the number of malpractice claims in civil arenas that had been opened with NDs, and they reported there were none in the 5 years that they covered NDs. Additionally, the committee contacted Jury Verdicts Northwest for data on civil claims against NDs, in the region with the greatest density of NDs (Oregon and Washington). Going back to 1919, their data reported that there was not one claim for prescribing negligence ever documented against a ND.

Ultimately, the formulary committee identified that the current furnishing laws, which required MD supervisory of ND drug furnishing, were essentially untenable. The number of MDs who have sufficient training and understanding of ND philosophy was limited and thus few could act as appropriate supervisors for NDs.

Additionally, the relatively few numbers of MDs, that were both willing and well-trained to manage ND supervision, were ultimately finding it impossible to obtain coverage from their current malpractice providers, when they were acting in a supervisory role to a ND. Research by the committee found a significant reluctance by the major medical malpractice carriers to even consider ND-riders which would allow for coverage for these MDs.

Alternatively, MDs are routinely covered by their malpractice insurers for their supervision of nurse practitioners and physician assistants. Ironically, these classes of practitioners have less entry-level training and educational requirements than NDs.

While NDs maintain their own malpractice insurance policies, it was deemed that currently it would be impossible for a MD to supervise a ND while being covered by his/her malpractice coverage.

With this in mind, this committee of pharmacists, MDs and NDs, developed a formulary of drugs that they deemed was appropriate for NDs to prescribe (rather than furnish with MD supervision). This formulary was developed by drug category and classification, similar to that organized by The *Drug Facts and Comparisons* publication. It was also suggested that the Bureau or a committee of the Bureau would monitor and manage updates to the formulary through department regulation rather than repeated lengthy statutory processes. Ultimately, the committee recommended that the statutes be changed to abolish the untenable furnishing provision and concurrently adopting the suggested formulary.

Lastly, the committee identified that the language in section 3640 needed to be clarified to appropriately authorize NDs to utilize the route of IV and IM since various legal interpretations were currently in place. An IV formulary and post graduate IV training course was crafted by the committee and recommended as an effective means to oversee and regulate ND use of the IV route.

At the time of this article, there is no legislative bill in place to address these committee recommendations.

Summary

Naturopathic doctors have existed as a continuously licensed profession for an honored period of time. While naturopathic doctors introduction into the licensed ranks in the State of California occurred only in the last few years, the impact to the medical community relegates that professions such as pharmacists need to acquire a knowledge base to the philosophy of this new class of prescribers, and foremost, to develop a concrete understanding to the scope of practice that governs the ND's prescribing and furnishing privileges.

NDs in the State of California enjoy limited prescribing privileges, yet fundamentally have the capabilities of furnishing all drugs (with the exception of CII Schedule drugs), provided they possess the appropriate licenses and have established an MD supervisory protocol, similar to that governing the furnishing practices of nurse practitioners. The statutes governing ND's prescribing were identified as limiting to the safe practice capabilities of NDs and, in many circumstances, untenable. Findings and recommendations by a committee of the Bureau of Naturopathic Medicine have suggested a drug formulary to expand the prescribing authority of NDs.

References

A few of the many suggested references, that would help expand the pharmacists knowledge base on the naturopathic doctor profession can include:

Profile of a Profession: Naturopathic Practice

www.futurehealth.ucsf.edu/pdf_files/Naturo2.pdf

Bureau Findings and Recommendations

http://www.naturopathic.ca.gov/about_us/reports.shtml

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Homeopathy
History, Manufacture, Research

by Simon Barker, N.D.

Homeopathy is one of the best known - and least understood - forms of alternative medicine. It has been established as a system of healing since the late 18th century, a time when conventional medicine included bleeding for fevers and mercury for syphilis.[1] The practice of homeopathy was so popular among medical physicians in the mid-19th century that MDs who didn't practice it formed their own body, the American Medical Association (AMA), in order to exclude those who did.[2] Homeopathy has long been the bane of conventional physicians, not least because of the perceived absurdity of the minuteness of the doses given. Many of the remedies are diluted beyond Avogadro's number - the point beyond which no molecule of the original substance is likely to be present in a given sample.[3] Whatever the objections from conventional physicians, even today, a number of placebo-controlled double-blind studies - the gold standard of allopathic medicine - have shown that homeopathy is effective in treating a variety of conditions.[4-9]

Homeopathy's founder, a German physician named Samuel Hahnemann, became fascinated with trying to understand the mechanism of action of quinine in treating malaria. So, he took a small quantity himself and found that he developed symptoms similar to those seen in malarial patients. He then surmised that a substance that can cause certain symptoms in a healthy person can cure them in a sick person.[1] For example, a bee sting causes redness, heat and swelling; one might consider using a homeopathic preparation from bees to treat an arthritis that involved red, hot, swollen joints. Hahnemann recognized his debt to other physicians such as Hippocrates and Paracelsus, but was the first to build a system of medicine around the notion of "like cures like." The job of the practitioner, in terms of *Classical* homeopathy, is to find the one remedy that most closely matches the symptoms of the patient - and this is how most homeopaths still practice.[1] Homeopathy is an individualized process - treating the patient, not the disease. Since Hahnemann's time, numerous other people have brought their ideas to homeopathy. Several, most notably Rudolf Steiner, have developed systems that often involve giving complexes of remedies together, usually in low potencies.

The job of the practitioner, in terms of classical homeopathy, is to find the one remedy that most closely matches the symptoms of the patient.

Homeopathic remedies are prepared or *potentized* by a process of serial dilution and shaking or *succussing*. If the dilution is 1:10, the remedies are called X or D (e.g. 6X or D30). If the dilution is 1:100, the remedies are called C (e.g. 200C). 1000C is commonly referred to as 1M. If the dilution is 1:50,000, the remedies are called LM (e.g. LM1). Remedies that are closer to material substance (e.g. 12X) are considered lower doses and remedies that are more dilute (e.g. 10M) are considered higher doses. The remedies are shaken between each dilution.[10] Remedies can be made from anything but are generally produced from natural substances - minerals such as salt (Natrum muriaticum), plants such as poison oak (Rhus *toxicodendron*) and animals such as the honeybee (Apis *mellifica*). Some remedies called *nosodes* are made from diseased human tissue (e.g. Psorinum, which is made from the skin of a scabies patient).[11] The names are typically given in their Latin designation. Most substances are crushed and mixed with lactose or dissolved in alcohol before dilution in distilled water. The finished product is most often sugar pellets treated with an alcoholic extract of the appropriate dose of the substance, although some remedies are taken as liquids. The pellets are typically allowed to dissolve on or under the tongue, away from food. In the United States, homeopathic medicines are classified

as over-the-counter drugs and regulated by the Food and Drug Administration (FDA) under the Homeopathic Pharmacopoeia of the United States (HPUS).[1]

Homeopathy is used all over the world by a vast number of people. 64% of people in India trust in homeopathy and it is estimated that there are a quarter of a million practitioners of homeopathy in that country alone.[12] The majority of these are medical physicians. Although there are many NDs, MDs and DOs using homeopathy in the United States, the majority of homeopathic prescribers are *lay* homeopaths, individuals without medical degrees who work solely or primarily with homeopathic remedies. In the United States, as in most countries, access to homeopathic drugs is not limited to physicians. According to a 1999 study, 6 million people in the U.S. use homeopathy each year. Homeopathy has been championed by many famous people from Gandhi to Rockefeller to David Beckham.[13]

The mechanism by which homeopathy works remains unclear. Much has been made of the notion of the "memory of water," as suggested by Jacques Benveniste, although repeated attempts to reproduce his research have had mixed results.[14] It is not necessary, of course, to understand the process for the medicine to be effective. Many pharmaceuticals, such as antiepileptics gabapentin and lamotrigine, have unknown mechanisms of action.[15] Most homeopaths believe, as did Hahnemann, that the remedies act not on the physical body directly but via an energetic body, what Hahnemann dubbed the *vital force*, stimulating the body's own healing properties.[16] This notion is analogous to that of *chi* in Chinese medicine and *prana* in Ayurveda.

Homeopathy was one of the earliest forms of scientific medicine. It was based on placebo-controlled trials. Hahnemann and his followers believed strongly in the importance of scientific observation and the foundation of homeopathic practice is the *proving* or blinded testing of homeopathically prepared medicines on healthy subjects to determine the specific qualities of that remedy. Effects beyond that of a placebo have been shown in rigorous examinations of *provings*.[17]

It is a Herculean task to unravel the information on research into homeopathy. There have been many hundreds of studies performed, most of them indicating some benefit for homeopathic remedies. Even several rigorous meta-analyses have shown homeopathy to be more effective than placebo.[18-21] But not all studies are positive - and negative studies on alternative medicine tend to get a lot of press.[22] Still, there are randomized controlled trials that show benefit for the homeopathic treatment of fibromyalgia,[4,23] osteoarthritis,[24-25] allergies,[5] otitis media,[7] sinusitis,[6] bronchitis,[26] PMS,[9] ankle sprain,[27] flu,[28] post-operative ileus,[29] chronic fatigue,[8] vertigo[30] and diarrhea.[31]

Despite the evidence, there is no consensus on homeopathic research. There are a number of reasons for this. First of all, there is a significant publication bias

Interest in homeopathy in the United States and worldwide is increasing.

against homeopathic research[32] and a strong tendency amongst conventional practitioners or researchers to editorialize within or without homeopathic studies.[33-34] Secondly, there is much disagreement about the way in which research into homeopathy is organized. The most important argument is probably that much of the research seeks to follow a traditional single drug model and does not represent the way in which the majority of practitioners use homeopathy.[33-34] Those which closely resemble this, such as the work of Dr. Jennifer Jacobs on childhood diarrhea,[31] tend to show significant benefit. It has also been argued that, because of the positive benefits of the long and detailed visit with a homeopath, the added benefits of the remedy may be difficult to tease apart from the therapeutic effect of the doctor-patient interaction.[35-36] Some suggest that the best way to go is to compare homeopathic treatment with conventional treatment. Such studies have often shown good results.[24-25,30] Many animal studies also show fascinating results. Homeopathic arsenic can aid rats poisoned by the same metal,[37] dogs with babesiosis respond as well to a homeopathic remedy as they do to conventional drugs[38] and homeopathy can slow the progression of prostate cancer in rats.[39] Animals, of course, do not have placebo responses. Meanwhile, recent research into newer antidepressants suggests that their actions are no greater than placebo for most depressed patients.[40] Ironically, the American Psychiatric Association President-elect countered that the studies did not accurately represent how physicians use the medications.[41]

At the end of the day, most of the opposition to homeopathy rests on its improbability rather than any lack of merit. Interest in homeopathy in the United States and worldwide is increasing. There are no known side-effects; it is cheap and non-invasive and there is a growing body of scientific evidence supporting its use.[1] Homeopathic remedies are prescribed by many licensed physicians. Understanding the principles behind the manufacture and administration of homeopathic drugs improves communication with physicians and their patients about the benefits and risks of using homeopathic remedies.

About the Author

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Integrating Natural Therapies for Women with Breast Cancer Undergoing Conventional Treatment

by Lise Alschuler, N.D., F.A.B.N.O.

Abstract: Characteristics of breast cancer and prevention/treatment concepts

Breast cancer, a disease of enormous significance to far too many women, is also fertile ground for integrative oncology. Over 80% of all people with cancer use some form of complementary medicine along with conventional care – compared to approximately 30% of the general population.[3] Unfortunately, only one third of individuals taking supplements inform their physician about the natural medicines that they are taking. Thus, it often falls to the pharmacist or other integrative healthcare practitioners to advise patients on the concurrent use of natural products with conventional cancer treatments. This review highlights several examples of natural therapies that reduce adverse toxicity and/or increase tumoricidal activity of selected breast cancer chemotherapeutics.

Breast cancer is fertile ground for integrative oncology. Among women, the three most common cancers are lung, breast and colorectal in developed countries and breast, cervical and stomach cancer in developing countries. In the United States during the year 2007, an estimated 178,480 new cases of breast cancer were diagnosed in women (representing 26% of all new cancer diagnoses in women), and 2,030 new cases of breast cancer were diagnosed in men. Also in the United States, an estimated 40,910 deaths from breast cancer occurred, with women making up 40,460 of those deaths (15% of all deaths due to cancer) and men comprising the remaining 450 deaths.[1] The estimated five-year relative survival rate for localized breast cancer is 98%, whereas the five-year relative survival rate for breast cancer that has spread regionally is 83% and for breast cancer that has metastasized to distant sites, the five-year relative survival rate is 26%.[2] Survival after breast cancer diagnosis has improved due to both earlier diagnosis and advances in conventional treatment. Survival after breast cancer diagnosis is also impacted by the incorporation of integrative therapies. In one study, breast cancer patients were twice as likely to report using complementary therapies than were prostate cancer or gastrointestinal cancer patients.[4] Among a Massachusetts cohort of women with early-stage breast cancer, 60% used megavitamin therapy along with surgery, chemotherapy, and/or radiation therapy.[5] Because only 1/3 of individuals taking supplements inform their physician about the natural medicines that they are taking, it often falls to the pharmacist or other integrative healthcare practitioners to advise patients on the concurrent use of natural products with conventional cancer treatments.[6]

Women with advanced breast cancer will typically receive combination chemotherapy treatment. Chemotherapeutics used to treat breast cancer include: doxorubicin (Adriamycin), cyclophosphamide (Cytoxan), docetaxel (Taxotere) paclitaxel (Taxol), paraplatin (Carboplatin), fluorouracil (5-FU), methotrexate (Amethopterin, Mexate, Folex), epirubicin (Ellence) and capecitabine (Xeloda). Additionally, antiestrogen therapies such as tamoxifen (Novaldex), letrozole (Femara), and anastrazole (Arimidex) are often employed in the treatment of Estrogen Receptor positive (ER+) breast cancer. These chemotherapeutic and antiestrogen agents present significant adverse toxicity (summarized in Table 1). Many women seek to manage this adverse toxicity with the use of natural supplements. Additionally, women seek natural therapies that will enhance the tumoricidal effects of chemotherapy agents. An evidence-based understanding of which natural supplements are indicated for these chemotherapy agents will best enable pharmacists to advise women with breast cancer in an effort to optimize their experience of, and outcomes from, conventional cancer treatment.

Doxorubicin, an antineoplastic anthracycline, is a typical first line chemotherapy agent, used in combination with cyclophosphamide. Doxorubicin is an intravenous medication. Adverse toxicity includes pancytopenia, stomatitis, nausea and vomiting, cardiotoxicity and facial flushing. Natural supplements that may help to reduce the toxicity of doxorubicin and well as enhance

its tumoricidal activity include: L-carnitine, CoQ10 (ubiquinol), Camellia sinensis (Green tea), and melatonin. L-carnitine interacts with cardiolipin, modifying membrane permeability and protecting the functions of the mitochondria. This mechanism may explain the protective effects of L-carnitine against doxorubicin induced cardiotoxicity.[7] Carnitine also exerts hepatoprotective effects against doxorubicin toxicity.[8] Coenzyme Q10, an essential component of the electron transport system and a potent intracellular antioxidant, helps to prevent damage to the mitochondria of the heart, thus preventing the development of anthracycline-induced cardiomyopathy. Studies further suggest that coenzyme Q10 does not interfere with the antineoplastic action of anthracyclines and might even enhance their anticancer effects.[9] Although there are no human trials, preliminary in-vitro and animal in-vivo data indicates a beneficial relationship between green tea and doxorubicin. When doxorubicin was administered intraperitoneally to mice with implanted Ehrlich ascites carcinoma, a 25% reduction in tumor weight was observed. When mice ingested green tea during the time period of doxorubicin administration, a decrease of 37% in tumor weight was observed. The ingestion of green tea enhanced the doxorubicin-induced tumor inhibition by 2.5-fold. Additionally, the doxorubicin concentrations in the heart and liver did not increase with ingestion of green tea; in fact the doxorubicin concentration in the heart was less than the doxirubicin-alone group[10] green tea extract, theanine in particular, inhibits the efflux of doxorubicin selectively from tumor cells, thus reducing tumor cell chemoresistance.[11] When melatonin is combined with doxorubicin, there appears to be reduced doxorubicin-induced cardiotoxicity.[12] Melatonin also inhibits the proliferation of estrogen receptor alpha (ER*a*)-positive (MCF-7), but not ER*a*-negative (MDA-MB-231) breast cancer cells, thus suggesting a synergistic effect with doxorubicin.[13] A related doxorubicin compound, liposomal doxorubicin (Doxil) has been shown to offer better survival advantage when given with melatonin. The one-year survival rate and the objective tumor regression rate were significantly higher in patients concomitantly treated with melatonin than in those who received Doxil alone. The tumor response rate was 42/124 in the chemotherapy plus melatonin arm versus 19/126 in the chemotherapy arm only ($P < 0.001$). The one-year survival was 63/124 in the doxil plus melatonin arm versus 29/126 in the doxil arm only ($P < 0.001$). Moreover, the concomitant administration of melatonin significantly reduced the frequency of thrombocytopenia, neurotoxicity, cardiotoxicity, stomatitis and asthenia.[14] Natural supplements which should be avoided during doxorubicin therapy include N-acetylcysteine which may increase tumor cell resistance to doxorubicin, and Curcuma longa or curcumin extract which may interfere with the cytotoxicity of doxorubicin. This interference is explained by the fact that curcumin inhibits stress-activated protein kinase (SAPK). SAPK activation is necessary for cell death in response to exposure to certain forms of cell stress (including Adriamycin and Cytoxan) and defects in SAPK signaling promote cell survival.[15]

Fluorouracils, namely 5-fluorouracil (5-FU), is commonly included in breast cancer chemotherapy regimens. 5-FU is given intravenously. It can cause pancytopenia, diarrhea, stomatitis, photosensitivity, xerodermia, nausea, headache, malaise, confusion and hand-foot syndrome. There are a number of natural agents which may act synergistically with 5-FU to enhance its tumoricidal action. DHA (Docosahexaenoic acid) from fish or algae derived oil, enhances cytotoxic effects of 5-FU.[16] DHA also exerts protective effects against intestinal lesions produced by 5-FU but requires the joint administration of supplementary protein.[17] Synergistic inhibitory effects have also been demonstrated in-vitro between curcumin and 5-fluorouracil on the growth of the human colon cancer cell line HT-29.[18] Combining curcumin with 5-FU significantly increases growth inhibition of AGS

Table 1. Adverse toxicity of chemotherapeutics used in the treatment of breast cancer

Chemotherapy agent	N/V	Pancyto-penia	Peripheral Neuropathy	Fatigue	Stomatitis	Confusion/ Dizziness	Cardio-toxcity
doxorubicin	√	√			√		√
cyclophospha-mide	√	√		√			√
taxanes	√	√	√	√			
carboplatin	√	√	√	√	√	√	
fluorouracils	√	√		√	√	√	
methotrexate	√	√			√	√	
epirubicin	√	√		√			√
Anti-estrogens				√		√	

human gastric carcinoma cell line compared with either curcumin or 5-FU alone ($P < .05$), suggesting synergistic actions of the two agents.[19] Green tea extract, particularly epigallocatechin-3-gallate (EGCG), increases growth inhibitory effects of 5-FU in human head and neck squamous cell carcinoma cells when given orally to mice in doses comparable to human dosing.[20] Further evidence of green tea synergism with 5-FU is seen in the postoperative management of patients with familial polyposis. Treatment with 5-FU suppositories and green tea extract administered after surgery caused some regression of the polyps in the preserved rectal segment, and no rectal cancer developed in any of these patients.[21] There are no known contraindications to 5-FU.

Taxanes, consisting of docetaxel (Taxotere) paclitaxel (Taxol) are commonly-used chemotherapy agents in breast cancer regimens. Taxanes are delivered intravenously. Taxanes may cause pancytopenia, nausea and vomiting, diarrhea, anorexia, arthralgia, peripheral neuropathy, myalgia, edema and fatigue. Again, several natural agents are indicated as a way to minimize the signficiant adverse toxicity from taxanes. One of the most indicated natural agents with taxane therapy is L-Glutamine. In a randomized clinical trial, 10 grams of L-Glutamine was given orally three times daily for 4 days starting 24 hours after completion of paclitaxel administration. There was a statistically significant reduction in the severity of peripheral neuropathy as measured by development of moderate to severe dysesthesias and numbness in the fingers and toes ($P < 0.05$). The degree and incidence of motor weakness was reduced (56% versus 25%; $P = 0.04$) as well as deterioration in gait (85% versus 45%; $P = 0.016$) and interference with activities of daily living (85% versus 27%; $P = 0.001$). Melatonin is another important natural agent to consider. In an open trial, melatonin was shown to increase the efficacy of single-agent Taxol in women with breast cancer, and to significantly reduce the frequency of thrombocytopenia, neurotoxicity, cardiotoxicity, stomatitis and asthenia.[23] Vitamin E as alpha-tocopherol, may reduce the peripheral neuropathy symptoms caused by taxanes. A clinical trial of 31 patients with cancer receiving six courses of cumulative cisplatin, paclitaxel, or combination regimens were randomized to receive oral vitamin E ($n = 16$) at a daily dose of 600 mg/day during chemotherapy and for 3 months after its cessation or received no supplementation ($n = 15$) to serve as controls. The incidence of neurotoxicity differed between the two groups, occurring in 25% patients assigned in the vitamin E supplementation group and in 73.3% patients assigned in the control group ($p = 0.019$). Mean peripheral neuropathy scores were 3.4 +/- 6.3 for patients receiving vitamine E and 11.5 +/- 10.6 for patients that did not receive vitamin E ($p = 0.026$).[24]

Tamoxifen, illustrative of anti-estrogen therapy, is used in the majority of breast

Table 2. Synopsis of natural therapies for selected cancer chemotherapy agents

Doxorubicin	Fluorouracils	Taxanes	Tamoxifen
L-carnitine (1g – 2g) CoQ10 (100mg – 300mg) Green tea (stnd. Extract to over 80% polyphenols with 50% EGCG; 1g – 2g) Melatonin (20mg)	DHA (400mg – 600mg) Curcumin (stnd. Extract with 95% curcuminoids; 1g – 6g) Green tea (stnd. Extract to over 80% polyphenols with 50% EGCG; 1g – 2g)	L-Glutamine (30g) Melatonin (20mg) Vitamin E (400i.u. – 800i.u.) Niacin (1200mg – 3000mg)	Riboflavin (200mg-400mg) CoQ10 (100mg-300mg) Hesperidin-methyl-chalcone (500mg - 1,500mg) Vitamin E (400i.u. – 800i.u.) Melatonin (20mg)

Table 3. Predicted herbal-chemotherapeutic interactions mediated through cytochrome activities

Botanicals	Chemotherapy drugs	Cytochrome enzymes	Expected effect on drug
Echinacea purpurea (coneflower)	Cyclophosphamide	2C8, 2C9, 2C19	Increased exposure
Ginkgo biloba (ginkgo)	Ifosfamide	3A4	Decreased exposure
Harpagophytum procumbens (Devil's claw)	Dacarbarzine	1A2	Increased exposure
Hypericum perforatum (St. John's wort)	Paclitaxol	2C8, 3A4	Decreased exposure
Mentha piperita (peppermint)	Docetaxel	3A4	Decreased exposure
Piper methysticum (kava-kava)	Vinblastine	3A4	Decreased exposure
Polygonum multiflorum (Fo-ti root)	Vincristine	3A4	Decreased exposure
Tanacetum parthenium (feverfew)	Navelbine	3A4	Decreased exposure
Trifolium pretense (red clover)	Etoposide	3A4	Decreased exposure
Schisandra chinensis (wu wei)	Irinotecan	3A4, 3A5	Decreased exposure
Valeriana officinalis (valerian)	Topotecan	3A4	Decreased exposure
	Tamoxifen	3A4, 1A2	Decreased exposure
	Armidex	3A4, 1A2, 2C8-9, 2C19	Decreased exposure
	Aromasin	3A4, 1A2, 2C8-9, 2C19	Decreased exposure
	Femara	3A4, 1A2, 2C8-9, 2C19	Decreased exposure
	Iressa	3A4	Decreased exposure

cancer patients. The main adverse effects of tamoxifen and other anti-estrogens are the production or aggravation of hormonal deficiency symptoms such as vasomotor flushing. The importance of tamoxifen in contributing to longer term survival also indicates the need for compounds which will enhance its efficacy. Preclinical data indicates that tamoxifen treatment is most effective during co-administration of riboflavin, niacin and CoQ10.[25] Hesperidin methyl chalcone (HMC) and vitamin E may be effective in helping to control vasomotor flushing.[26] Concomitant administration of melatonin may induce objective tumor regressions in metastatic breast cancer patients refractory to tamoxifen alone as demonstrated in a phase II clinical trial.

The examples of natural supplements described in this review illustrate the benefit that natural therapies may provide women with breast cancer who are undergoing chemotherapy. The chemotherapy agents and indicated supplements are summarized in Table 2. It is always important to consider potential negative interactions as well. Most of these are theoretical and based upon postulated cytochrome enzyme up- or down-regulation (see Table 3.). Nonetheless, a prudent approach would avoid use of any potentially deleterious supplements. Overall, there are many supplements which may improve the quality and quantity of life for women with breast cancer receiving chemotherapy and hormonal therapy. Pharmacists have the opportunity to guide these women to incorporate the most safe and successful natural therapies.

About the Author

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Dr. Alschuler is a naturopathic physician with board certification in naturopathic oncology. Dr. Alschuler has been in practice for over 14 years. Dr. Alschuler is the current President of the American Association of Naturopathic Physicians, member of the American Board of Naturopathic Oncology Board of Medical Examiners, and immediate past-President of the Illinois Association of Naturopathic Physicians. Dr. Alschuler provides naturopathic oncology at Naturopathic Specialists in Scottsdale, AZ. Previous to this, she was Director of naturopathic medicine at Cancer Treatment Centers of America, a JCAHO accredited regional hospital specializing in comprehensive integrative cancer located north of Chicago. Dr. Alschuler co-authored The Definitive Guide to Cancer: An Integrative Approach to Prevention, Treatment and Healing (Celestial Arts, 2007). She has presented at numerous professional conferences, and continues to give presentations for lay and professional audiences. She has received professional recognition and many awards for her work in integrative medicine.

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Drug Interactions and Nutrient Depletions

by Chris D. Meletis, N.D.

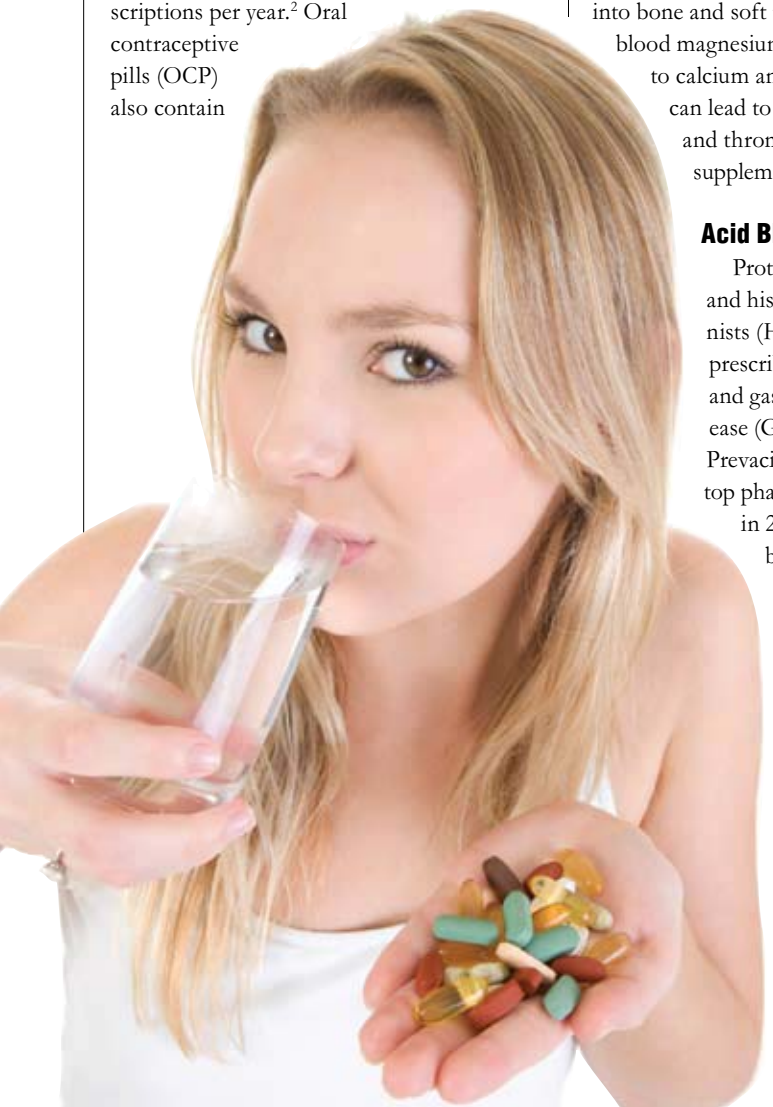
According to the Centers for Disease Control, the number of adults aged 55-64 taking at least one pharmaceutical in the last month rose from 62 percent in 1988-1994 to 73 percent in 1999-2002.[1] The large number of individuals taking pharmaceutics suggests that the potential for drug-nutrient interaction is substantial. The following discussion looks at common medications and the nutrient depletion considerations.

Common Pharmaceuticals that Deplete Nutrients

Hormone Replacement

In the U.S. from 1999 to 2002, approximately 15 million women were taking HRT annually accounting for 90 million prescriptions per year.[2] Oral contraceptive pills (OCP) also contain estrogen/progestin combinations. Research suggests that estrogens significantly deplete several B vitamins. Oral estradiol decreases pyridoxines (vitamin B6) as well as albumin in postmenopausal women.[3] This vitamin B6 deficiency is believed to be associated with a disruption in tryptophan metabolism.[4] Proper tryptophan metabolism is essential for serotonin production, which is essential for proper mood stabilization and contentment in life.

Additional research indicated that oral contraceptives deplete riboflavin (vitamin B2), folic acid, cobalamin (vitamin B12), ascorbic acid (vitamin C), and zinc.[5] Studies indicate a decrease by 40 percent of both folic acid and serum B12 levels with oral contraceptive use.[6] Additionally, studies have shown that estrogen supplementation increases magnesium uptake into bone and soft tissue, causing lowered blood magnesium levels. This change leads to calcium and magnesium changes and can lead to an increase in coagulation and thrombosis seen with estrogen supplementation.[7]



Acid Blockers

Proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2 blockers) are commonly prescribed for treatment of ulcers and gastroesophageal reflux disease (GERD). Lansoprazole, or Prevacid, is a PPI ranking third in top pharmaceutical sales in the U.S. in 2004.[8] Acid blockers have been linked to significant increases in the risk of vitamin B12 deficiency.[9] One small study showed a 53 percent decrease in protein-bound B12 absorption in individuals taking an H2 blocker.[10] Research also indicated that folic acid absorption is decreased with supplementation of H2 blockers and other antacids.[11] Studies have also linked H2 blockers, which decrease gastric acid secretion, with decreased absorption of iron and zinc.[12-13] One study showed a direct correlation between increasing dosage of cimetidine, an H2 blocker, and decreasing dietary non-heme iron absorption ranging from 28-65 percent.[14] Animal studies also have demonstrated that cimetidine significantly decreases intestinal calcium transport.[15] In addition, it also alters vitamin D metabolism by altering the enzyme vitamin D 25-hydroxylase activity.[16] A small study performed with the PPI omeprazole demonstrated that serum levels of beta carotene were decreased with increased gastric pH.[17]

Corticosteroids

Corticosteroids are frequently prescribed for anti-inflammatory and immunosuppressant activity. Prednisone and hydrocortisone are often prescribed for various medical conditions such as autoimmune diseases and inflammatory conditions. Corticosteroid treatment has been associated with increased loss of bone mineral density. Studies show that these drugs decrease calcium absorption and increase calcium excretion.[18] Also, a study with individuals with chronic airway obstruction showed long term oral steroid therapy is associated with decreased serum magnesium levels.[19] Steroid medication has also been associated with low potassium in both animal and human studies.[20-21]

Studies in individuals with rheumatoid arthritis (RA) showed serum levels of zinc and copper are two other nutrients that suffer declines after corticosteroid treatment, and urinary excretion of zinc and copper is elevated.[22] Additional studies on patients with RA receiving corticosteroid therapy also demonstrated a decrease in plasma selenium levels.[23] Although the evidence appears incomplete or conflicting, some studies suggest that vitamin C and vitamin D may be affected by corticosteroid therapy.[24-25]

Aspirin

Aspirin is used for antipyretic, analgesic, and anti-inflammatory activity. Recent promotion of aspirin as prophylactic treatment to

decrease platelet aggregation to prevent transient ischemic attacks, stroke, and thromboembolism has increased the use of this over-the-counter medication.[26] Treatment with aspirin, or acetyl salicylic acid, affects several nutrients. Multiple studies have shown that aspirin therapy decreases vitamin C absorption.[27] Some studies also indicate that increasing aspirin dosage directly correlates to increasing ascorbic acid excretion in the urine.[28] Research also suggests that aspirin therapy causes an increase in gastric blood loss leading to a decrease in total body iron.[29] Evidence also supports that supplementation with aspirin significantly decreases both total and bound-serum folate and slightly increases folic acid excretion.[30]

Anti-Diabetic Drugs

According to the American Diabetes Association 2005 statistics, approximately seven percent of the U.S. population is diabetic. They estimate that 57 percent of adult diabetics take oral medication only and an additional 12 percent take insulin plus oral medication to manage the condition.[31] Metformin, a frequently prescribed biguanide, has been shown to deplete vitamin B12 and folic acid. Studies indicate that long term metformin therapy significantly decreases serum vitamin B12 levels. Additional studies suggest that short term treatment with metformin increases homocysteine levels, and supplementation with B vitamins or folic acid can moderate this response.[32] More specifically, serum folic acid levels have been shown to decrease 7 percent and vitamin B12 levels decrease by 14 percent with metformin therapy in type 2 diabetic individuals.[33] Although limited, research also suggests that treatment with sulfonylureas (e.g. Glipizide Gliclazide glyburide, Glimepiride, etc.) increase the risk of CoQ10 deficiency.[34]

Statin Drugs

The statin drug Lipitor® is one of the top selling pharmaceuticals worldwide and brought in an estimated 12.2 billion dollars in sales to Pfizer in 2005.[35] Statins inhibit the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA reductase), which decreases cholesterol synthesis by inhibiting the conversion of acetyl CoA to mevalonate. Mevalonate is also necessary in the production of ubiquinone, or coenzyme Q10 (CoQ10). Numerous studies have demonstrated that statin drug therapy significantly decreases plasma levels of CoQ10.[36] CoQ10 is necessary for mitochondrial energy production as well as exhibits potent antioxidant activity.[37] Some researchers suggest that the depletion of COQ10 could account for some side effects associated with statin drugs such as myotoxicity and hepatotoxicity.[38-39]

TABLE 1. Symptoms of Nutrient Deficiency

Biotin	Alopecia, depression, dermatitis, nausea, anorexia
Calcium	Rickets, osteoporosis, osteomalacia, muscle spasms
Carnitine	Muscle weakness, poor lipid metabolism, failure to thrive in children
Cobalamin	Anemia, fatigue, poor nerve function, diarrhea
Coenzyme 10	Hypertension, fatigue, cardiovascular diseases
Folate	Anemia, fatigue, cervical dysplasia, diarrhea, gingivitis, depression, irritability, insomnia
Iron	Anemia, weakness, fatigue, poor immune function
Magnesium	Fatigue, irritability, weakness, muscle cramps, insomnia, anorexia, poor nerve conduction
Niacin	Pellegra, dermatitis, confusion, diarrhea
Pantothenic acid	Fatigue, numbness and pain in the feet
Potassium	Fatigue, irregular heart beat, irritability, confusion, poor nerve conduction
Pyridoxine	Depression, fatigue, dermatitis, anemia, glucose intolerance
Riboflavin	Cheilosis, gisossitis, dermatitis, visual disturbance
Selenium	Keshan disease, poor immune function
Thiamine	Beriberi, depression, memory loss,numbness, fatigue
Vitamin C	Scurvy, decreased immunity, poor wound healing
Zinc	Slow wound healing, decreased immunity, loss of taste and smell, alopecia, skin disorders

Antihypertensives

Common antihypertensive medications include beta-adrenergic blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and vasodilators. According to the American Heart Association, an estimated 65 million Americans, almost one in three adults, has high blood pressure.[40] Vasodilators such as hydralazine deplete vitamin B6.[41] Captopril, an ACE inhibitor, has been shown to cause hyponatremia by increasing sodium excretion and may cause hyperkalemia.[42-43] Also, studies with the beta blocker propranolol have shown that the drug inhibits the CoQ10 enzymes in myocardium.[44]

Diuretics

Diuretics are known for altering certain nutrient levels such as potassium. However, many other nutrients are affected. Thiazide diuretics have been shown to deplete magnesium, sodium, potassium, and zinc. One study found hyponatremia in 13.7 percent and hypokanemia in 8.5 percent with individuals treated with thiazide diuretics.[45] Thiazide diuretics also decrease magnesium in approximately 20 percent of patients.[46] Additionally, research indicates that thiazide diuretics cause significantly decreased serum zinc.[47] Loop diuretics have been shown to deplete potassium, magnesium, calcium, zinc, pyridoxine, thiamine, and ascorbic acid. One study found that thiamine deficiency was found in 98 percent of congestive heart failure patients receiving 80 mg of furosemide per day and in 57 percent of those receiving 40 mg per day.[48] Ascorbic acid and pyridoxine excretion are also increased with furosemide treatment.[49] Additionally, several studies demonstrate that loop diuretics increase the excretion of sodium, potassium, calcium, magnesium, and chloride.[50]

Conclusion

Drug-induced nutrient depletion can lead to potential further health challenges. Visiting with your health care provider and pharmacist about how to minimize these potential

TABLE 2. Pharmaceuticals and Nutrient Depletion	
Acid Blockers	CoQ10, cobalamin, folic acid, iron, vitamin D, beta carotene, zinc
Antibiotics	B vitamins, vitamin K, magnesium, calcium, potassium, zinc, iron
Anticonvulsants	Biotin, thiamine, cobalamin, folic acid, CoQ10, vitamin D, vitamin K, calcium, carnitine
Anti-Diabetic Drugs	Cobalamin, folic acid, CoQ10
Antihypertensives	Pyridozine, sodium, CoQ10
Aspirin	Ascorbic acid, iron, folic acid
Corticosteroids	Calcium, magnesium, potassium, zinc, copper selenium, ascorbic acid, vitamin D
Diuretics	Thiamine, pyridoxine, ascorbic acid, potassium, magnesium, calcium, zinc, sodium
Estrogen/ progestins	Riboflavin, pyridoxine, cobalamin, folic acid, ascorbic acid, zinc, magnesium
Statins	CoQ10

nutritional-deficit side effects is essential. When managing drug therapy, keeping your doctor or other medical professional in the "loop" is critical.

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Prescription Pharmaceuticals, Herbal Medicines and Nutritional Supplements

A Review of the Crucial Concepts

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Why Use Herbs or Supplements?

The reality facing pharmacists and all other health care practitioners today is that the general public is using more and more herbal medicines and nutritional supplements. To understand why simply discontinuing these supplements during a pharmaceutical regimen may not be in the best interest of the patient, I am going to introduce some terminology from *Oriental Medicine* (OM) in order to broaden the understanding of why it may be advantageous to combine them.

OM theory discusses health from the standpoint of a balance in the body of Qi, or energy; yin and yang, opposite polar qualities that apply to everything (hot/cold, wet/dry, etc.); or one of the primary body fluids: blood and essence. When the body's qi, yin and yang, and body fluids are in balance, normal health is the result. When these become imbalanced for some reason, disease will result. Imbalancing factors can include improper nutrition, excesses of poor quality food and drink, emotional factors, or an invasion of the body by external pathogenic influences. When analyzing a case from the OM perspective, every illness can be defined as either an excess condition, or a deficiency condition. For example, in a deficiency case the most fundamental root cause can be a lack in the body of qi, blood, essence, yin or yang. Likewise, an excess case has, as its root cause, an excess of one of these qualities, or possibly an excess of external pathogens.

Treatment from the OM perspective would fall into one of two categories. For excess conditions, the treatment involves clearing out whichever factor is present at excess levels. Treatment of a deficiency case, likewise, would focus on replacing the deficient levels of the missing factor. For example, a case of hypertension from the OM perspective could be caused either by an excess of yang, usually leading to a stagnation of qi and a buildup of excess heat; or be caused by a deficiency of yin, which would mean that the normal levels of yang in the body are not balanced, giving the appearance of a yang excess. The symptom of hypertension will result in either case, but the root cause is different. The yang excess hypertension is treated by clearing yang. The yin deficiency hypertension is treated by replacing, or tonifying, the yin. [7]

Tonification is a concept that is included in many systems of alternative medicine, such as oriental medicine and naturopathic medicine. It is not, however, a significant part of mainstream western medicine. The concept of tonifying can also be thought of as rebuilding. Herbal remedies and other supplements can be targeted to specific organs as well as the whole body.

Western pharmaceutical drugs, when analyzed as a group, almost entirely would be agents that would treat excess conditions. In other words, they are designed to suppress symptoms by clearing excesses. Very few, if any, pharmaceutical drugs would meet the requirement of treating deficiency conditions by tonifying.

Herbal medicines, depending on the specific herbs and how they are used, can treat either excess or deficiency cases. The most frequently used herbal medicines tend to be the herbs which treat deficiencies through the process of tonification, primarily because this is a treatment aspect which western pharmaceutical drugs tend to be missing. When patients are sick with an excess condition and need to have a suppressive treatment, western drugs are very often an effective approach. When the average patient is suffering from a deficiency illness, however, western drugs will usually not be effective, especially for the long term. Similarly, nutritional supplements, as a group, are almost entirely used to treat deficiency conditions (a few specific supplements with more antimicrobial properties aside). Vitamins, minerals, amino acids and other supplements are intended to replace levels of these nutrients that the individual appears to be lacking.

Resources for Assessing Herbal/Nutrient/Drug Interactions

There is actually a great deal of science available in the field of herb-drug and nutrient-drug interactions. Some of the major textbooks on this subject include:

- Herb, Nutrient and Drug Interactions: Clinical Implications and Therapeutic Strategies
  Stargrove, Treasure & McKee; Elsevier, 2008
- The Essential Guide to Herbal Safety
  Mills & Bone; Elsevier, 2005
- Herb Contraindication & Drug Interactions
  Brinker; Eclectic Medical Publications, 2001
- Interactions between Drugs & Natural Medicines
  Meletis & Jacobs; Eclectic Medical Publications, 1999
- Natural Standard
  Ulbricht & Basch; Mosby/Elsevier, 2005

Of these, the most reasonable, in terms of practical clinical experience is the Mills & Bone book, *Essential Guide to Herbal Safety.* Many books on the market have a tendency to rely too heavily on speculative, theoretical and unproven interactions, without accounting for what amounts in some cases to many hundreds of years of safe clinical use.

For a variety of reasons, it may be advisable for patients to continue their nutritional supplements in parallel with treatment with pharmaceutical drugs. Often patients will have various deficiencies and excesses present at the same time. Because of their ability to treat deficiency conditions, an ability most pharmaceutical drugs lack, it is often in the patient's best interest to continue an herbal or nutrient regimen in conjunction with their pharmaceuticals.

As seen in routine clinical practice, many patients who are experiencing the tonifying benefits of herbal or nutritional supplements are reluctant to discontinue them while taking prescription drugs. Many may continue them anyway, despite their MD's or pharmacist's warning not to. With this being the reality of patient care, learning to co-manage drugs and herbal/nutritional supplements safely should be the goal of every health care provider. The rest of this article is an overview of the basic concepts and resources available in this process.

Types of Interactions

Interactions can be divided into at least four categories,[2] with some authors listing five or even six.

a) Confirmed Interactions. These have been confirmed from multiple case reports and/or controlled trials. These may be due to actual interactions between chemical in the drug and chemicals in the herb, synergistic effects (both the herb and the drug performing the same physiological action, such as Ginkgo and aspirin), or an effect on the CYP450 system, to either inhibit clearing of the drug, leading to an increased effect, or accelerating drug clearance, causing a reduced drug effect.

b) Attributed. This category has some level of evidence which is suggestive of the interaction, though the level of documentation may not be definitive. This category is often sub-divided into probable, possible and unlikely.

c) Speculative or Theoretical. This may be due to an analysis of chemical constituents of an herb, and speculating it may behave in a manner similar to a drug based on the same chemical family. This category provides for the most confusion, since often these interactions are not proven in clinical practice. This category also includes interactions for which the only evidence is animal testing, especially if that testing is based on the injection of the herb or isolated compounds into test animals, often in dosages equivalent to humans consuming excess levels of the whole herb.

Western pharmaceutical drugs, when analyzed as a group, almost entirely would be agents that would treat excess conditions. In other words, they are designed to suppress symptoms by clearing excesses.

d) Inaccurate. This category refers to interactions that have been circulated, sometimes widely, in the phyto-pharmacological literature, that have since been shown to be inaccurate, and were based on erroneous information about the chemical constituents of the herb, the specific part of the plant used, perhaps, was based on a related plant species, or was simply theoretical in nature, but did not hold up when actually tested. Another category that should be included in this category are instances where tests of isolated compounds are shown to be problematic, are then inferred to apply to the whole herb, which usually contains dozens and sometimes hundreds of other compounds, many of which may have the opposite physiological effect.

As with any drug or even food, idiosyncratic reactions unique to the individual can also take place. These may be allergic, usually IgE mediated, or through some other immunological or physiological mechanism, and can be independent of any drug interaction. Regardless of the established safety of an herb or supplement, idiosyncratic reactions should always take precedent when evaluating a patient response, and the herb or supplement discontinued. Often, naturopathic doctors or other providers trained in the safe use of herbs and supplements can find an alternative to accomplish the same therapeutic objective that will not have the same side effects. [1,2]

Interactions of Key Supplements and Herbs

The following is a short review of some of the major herbs in common use, and a review of proven interactions. Selectively included are some theoretical or inaccurate interactions that may still be found in some of the older literature

Blood Thinners and Omega-3 Oils

Conventional tradition has been to limit the use of omega-3 fatty acids in patients taking blood thinners or when preparing for surgery. In a mini-meta analysis, Harris reviews 19 studies which concluded that there was no increase in bleeding risk between patients taking omega-3 oils concomitantly with aspirin, warfarin, or calcium channel blockers, and controls, for a variety of medical procedures including: coronary bypass operations, angioplasty, endarterectomy or coronary angiography. At present level of knowledge, which Harris sets at level A, Omega-3 fatty acid supplements, when dosed between 1-4 grams per day, do not increase the risk for adverse bleeding events even when used concomitantly with aspirin or warfarin. Newer anti-platelet drugs (clopidogrel, for example) have not yet been examined directly. [6]

Antibiotics and Probiotic Supplements

Antibiotics, especially repeated doses, will tend to damage or deplete intestinal flora that are crucial for normal GI health and immune system function. If taken concomitantly antibiotic agents will act on the bacteria present in probiotic supplements, leaving a smaller dose for systemic absorption and treating the target infection. One treatment approach has been to discontinue any probiotic supplement until after the

To maximize absorption of antibiotics, and minimize interactions between them and probiotic supplements, one effective treatment protocol is to administer doses of probiotics mid-way between doses of antibiotics.

course of antibiotic therapy, then resume - or start - a supplementation program to replace the gut flora destroyed during antibiotic treatment. Due to side effects of gas, bloating, diarrhea or systemic and vaginal yeast infections, overgrowth of *Clostridium difficile* leading to pseudomembranous colitis, all known side effects of antibiotic treatment, many patients will express a desire to continue probiotics during antibiotic treatment.

Current research shows that co-administration of probiotics during antibiotic treatment will prevent or eliminate antibiotic induced diarrhea. 500 mg of *Saccharomyces boulardii* bid helps prevent recurrence of *Clostridium difficile* infections secondary to antimicrobial therapy. Evidence for coadministration of probiotics and antibiotics is strongest for cases of diarrhea. Evidence is for preventing *C. difficile* infections is also good.[1]

To maximize absorption of antibiotics, and minimize interactions between them and probiotic supplements, one effective treatment protocol is to administer doses of probiotics mid-way between doses of antibiotics. For example, if taking antibiotics bid 12 hours apart, take the doses of probiotic six hours after the first dose of antibiotics.

Milk Thistle

Latin name *Silybum marianum*, the plant part most frequently used are the seeds. Historically, it was used to treat liver disease since at least medieval times. In the 1960s, German researchers isolated a flavolignan compound as one of the main active ingredients which was called Silymarin.[1] This has since become used in isolated form for many poisonings or cases of liver damage. Milk thistle is a frequently-used herb for supplements aimed at various liver conditions or detoxification.

Milk thistle is generally regarded in herbal medical circles as one of the safest herbs any patient could take. It is safe for use in both pregnancy and lactation, with no evidence of birth defects in both human and animal studies. There is only minimal evidence of any drug interaction.[2] Hence, reports that it can cause or exacerbate other illness should be treated cautiously. An example is a report that in one case study, milk thistle was found to exacerbate hemochromatosis in a patient with the C282Y homozygous form. The author's conclusion was that patients diagnosed with this genetic form of hemochromatosis should be cautious about taking milk thistle.

Analysis of the full text article, however, revealed that the patient had been concurrently taking extra-strength aceaminophen, 2 pills every 2-3 days. Acetaminophen is well documented as a possible source of liver damage. The milk thistle supplement was discontinued at the same time as the acetaminophen, yet the patient's subsequent improvement was attributed by the author entirely to the discontinuation of the milk thistle (ref 8). The evidence for the conclusion in this case was dubious at best, but does serve as an example of why care must be exercised and reliable sources utilized when dealing with herbal medicines.

Take Home Message

- Herbs and nutritional supplements have strong science behind them regarding drug interactions.
- In most cases, it is possible to choreograph delivery of herbs, supplements and drugs in a manner that will be both safe and efficacious.
- When necessary, it is usually possible to find substitute herbs or supplements that will accomplish the same treatment objectives with no interactions with the pharmaceutical drugs being used.
- The main advantage of combining supplements and herbs in a treatment program is that, while pharmaceutical drugs are excellent at symptom control, in many cases they do not correct an underlying root cause. Nutritional supplements and herbs, as part of a comprehensive program, often do address the root cause, and/or stimulate healing of organs, which will result in a higher state of long-term health.
- Helping the patients through the process of herb/nutrient/drug safety will build long-term rapport with the patients.
- As a profession, naturopathic doctors are heavily trained in the safe use of herbs and supplements, and how to combine them with prescription drugs in a manner that will ensure safety for the patient. Establishing a relationship with your local naturopathic doctor can be a beneficial relationship for pharmacists, naturopathic doctors, and patients.

Comfrey

Latin name *Symphytum officinalis*, comfrey is used in both gastrointestinal conditions as well as respiratory problems and to facilitate healing of broken bones or open wounds[9, 10] It is considered to be an excellent component in natural treatment of gastric and duodenal ulcers. Comfrey, however, along with related species *S. uplandicum*, Russian Comfrey, *S. asperimum*, Prickly Comfrey, and *S. tuberosum*, Scottish Comfrey contain chemicals known as Pyrrolizodine Alkaloids, or PAs. PAs in isolation have been shown to cause a type of liver damage known as Veno-Occlusive disease.

The only one of these plants with a tradition of medicinal use is *S. officinalis*. For this plant it is especially crucial to use only high-quality sources. The other Symphytum species have higher levels of PAs, and while mature adult leaves of *S. officinalis*, most frequently used as

tea, contain low levels of PAs, other species produce. Furthermore, there may be breakdown products, N-oxide derivatives of unsaturated PAs present, which can be more toxic than the PAs themselves. The non-medicinal strains appear to have higher levels of the N-oxides than does the pure comfrey strain.[12, 13]

When used appropriately, comfrey has been shown to be safe for short term use, and for selected individuals, even for long-term use. It is not recommended with pre-existing liver conditions.[11] Concerns about concomitant use of comfrey with pharmaceuticals should therefore rest the total toxic load, and whether or not any other pre-existing liver or kidney pathology is present.

Patients should be informed that for all of the traditional uses of comfrey, safe, herbal medicine options are available that will accomplish the same therapeutic objectives with less potential load or damage on the liver, if they need to take prescription medications for any length of time. The more medications they are on, the safer it will be to avoid comfrey at the same time as prescription drugs. These cases probably warrant a referral to a naturopathic doctor to find alternative herbal therapies.

It is important to reiterate, however, that when used appropriately, true comfrey, i.e., *S. officinalis*, has a long history of safe, effective use.

Echinacea

Several species of echinacea, aka purple coneflower, are a widely used anti-infective herbal medicine. The mechanism of action appears to be through upregulation of WBC levels, including NK cells, as well as enhanced cytokine production.[10, 14] Echinacea is safe during pregnancy and lactation.[1, 2] Interactions are possible with immunosuppressive drugs, by possibly making these drugs less effective. The evidence for this at present is theoretical. Since other natural treatments for cases of infection exist, the current standard is to avoid prescribing echinacea during courses of immunosupressive therapy. If the patients are interested, referral to a naturopathic doctor would be appropriate.

How to use this information

A reality is that most working pharmacists may not have the time to become experts in herbal medicines and nutritional supplements. Acquiring one or two of the resource texts listed earlier can permit you to look up some information quickly. If your patient base contains a large number of people asking questions about herb and nutrient safety, naturopathic doctors can be a tremendous resource. Most will willingly answer questions regarding herb/nutrient - drug interactions and safety. Visit the website of the California Naturopathic Doctors

Association (CNDA) to find the naturopathic doctors in your area and call or visit them. When patients have specific questions about herbs or supplements they are taking, and they will, calling your local naturopathic doctor can be a great way to build rapport with both the patients and your local naturopathic community. In the long run, this can be more in the patient's best interest than a knee-jerk response to "stop all your supplements and herbs," which many patients won't do anyway. Finding out how to combine them safely can facilitate future communication with the patient, who will be more comfortable their pharmacist is on board with their healthy lifestyle.

About the Author

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Black Cohosh

An Herbal Alternative for Menopausal Symptoms

by Janice Hoffman, Pharm. D.

Menopause and the Role of Estrogen

Menopause begins when a woman's menstrual cycle ends signaling the end of the reproductive years. However, prior to the onset of menopause, perimenopause begins a gradual decline of estrogen and progesterone during the late third to fourth decade of life. For some women, perimenopause can last only a few months and for others it can last ten years or more. On average, however, perimenopause lasts for 4 years. During the last couple of years of perimenopause, the decline of estrogen accelerates which can be related to a variety of symptoms. For the purpose of this paper, the reference to symptoms will be called menopausal to encompass perimenopause and menopause.

Menopausal symptoms are unique to each woman and may include:

- Memory problems
- Night sweats
- Hot flashes
- Mood swings, difficulty sleeping
- Fatigue
- Heart palpitations
- Lowering of the breasts
- Loss of bladder control with increased frequency
- Irregular menstrual period
- Vaginal dryness, decreased libido and pain with intercourse[1]

Approximately 40% of women seek medical advice for the management of their menopausal symptoms. Over the next decade, approximately 25 million women will approach menopause with many therapeutic choices available for the reduction of symptoms.[2] Estrogen is one choice for menopausal symptoms but the controversy of hormone replacement therapy continues due to the immediate benefits of symptom control with perhaps a reduced risk of heart attack and reduced chance of hip fracture but with long-term risks of cancer. Estrogen is actually a trio of hormones: estrone, estradial and estriol in a ratio 15/15/70.[1] Estrogen appears to increase the pliability of blood vessels, increase HDL, decrease LDL cholesterol and decrease platelet aggregation. In pre-menopausal women this may lower the risk of heart disease. However, the long-term risk of cancer (i.e. breast, ovarian, and uterine) related to hormone replacement therapy remains.[1] As an alternative to this, women may look towards natural products for their hormone replacement therapy.

Natural estrogen is defined as estrogen coming from a natural source and the composition is identical to that found in the body.[1] Horse's urine for example, is a source of estrogen, however it contains more estriol then the human female body. With the controversy regarding hormone replacement therapy with estrogen, many women are seeking alternative medicinal products to reduce symptoms of menopause with what consumers believe are less risk factors.

Black cohosh has become an increasingly popular herbal supplement for menopausal symptom control with herbal mainstream retail sales in 2000 ranking 14th in the United States.[3] The purpose of this article is to review the used of black cohosh for menopausal symptom reduction. Black cohosh is used as a dietary supplement and is regulated as a food not as a drug. Thus, manufacturers do not have to provide any evidence of efficacy or safety or quality control of the product prior to marketing.

Historical Perspectives and Uses of Black Cohosh

Black cohosh (Cimicifuga racemosa) is a member of the buttercup flower family and is plant native to the forests of eastern North America and has a strong unpleasant fragrance.[4] Black snakeroot, rattleweed, and squawroot are other names used for black cohosh. Bugbane is another common name used for black cohosh because it has been used as an insect repellent.

American Indians have used this plant to treat snakebites.[5] Early colonists used the root to treat a range of symptoms from general malaise and sore throat, to malaria, rheumatism, kidney disorders, childbirth, and menstrual abnormalities.[3] In the early 1900s black cohosh was used as a home remedy for fever, as a diuretic to bring on menstruation and for inflammation including rheumatism.[6]

An old time remedy called "Lydia Pinkham Vegetable Compound" contained black cohosh and was used for menstrual and menopausal symptoms during the early 1900s. Remifemin (GlaxoSmithKline) is the brand name for the plant extract that has been used in Germany since the 1950s for menopausal symptoms.

Black Cohosh in the Management of Perimenopausal Symptoms

Mechanism of Action:

The active components of black cohosh are derived from the understems (rhizomes) and root and include: phystosterin; isoferulic acid; fukinolic acid, caffeic acid; salicyclic acid; sugars, tannins; long-chain fatty acids and triterpene glycosides, including acetein, cimicifugoside and 27-deoxyactein.[7] The mechanism of action remains unclear and the effects on estrogen receptors if any, yields conflicting data.[6, 8] Recent research suggests black cohosh may have some effects as a partial agonist of 5HT-1A, 5HT-1D and 5HT-7 serotonin receptors and these effects may be related to neurotransmitter feedback loops.[9,7] Black cohosh also appears to increase blood flow to the pelvic area.[9] It is proposed that black cohosh might have selective estrogen receptor modulating effects and thus have estrogenic effects in some tissues and antiestrogenic effects on other tissues.[7] In animal models, there is some initial evidence suggesting that black cohosh may have estrogenic effects on the bone and Luteinizing Hormone (LH) but does not stimulate an increase in uterine weight.[7] Research on breast cancer cells suggest that black cohosh does not promote tumor growth but in animal studies seems to increase metastatic cancer in existing cancer.[7] Therefore, black cohosh should be avoided in women with existing breast cancer

or with a high-risk of developing breast cancer until further studies have been done.[7]

The duration of therapy for black cohosh is suggested to be limited to 6 months.[3,8,10] This is based on hormone replacement therapy recommendations for menopause in Germany and the United States to be limited to 6 months.[3]

Adverse Effects:

Side effects of black cohosh are rare
Most common:

- Gastrointestinal – nausea and vomiting at therapeutic dose
- Hypotension
- Overdoses can be associated with:
  - Dizziness
  - Visual disturbances
  - Reduced heart rate
  - Increased perspiration
- May induce miscarriage thus is contraindicated during pregnancy.

Serious:

- Hepatotoxicity (49 cases reported worldwide). There is some uncertainty as to this significance due to concomitant use of other medications.[11]

Potential Drug Interactions:

There is not sufficient data to determine if the following potential herb-drug and herb-dietary supplement interactions are clinically significant at this time, but drug interactions may include:

1. May interact with drugs metabolized by CYP3A4 enzyme system as a potent inhibitor of the CYP3A4 system[12]
2. Black cohosh used with cisplatin might have decrease cytotoxic effect of cisplatin on breast cancer cells based on animal models[7,13]
3. Black cohosh used with doxorubicin and doxcetaxel may have increased sensitivity to the cytotoxic effects based on animal models[13]
4. May interact with drugs metabolized by (CYP2D6) enzyme system - may modestly inhibit enzyme system[7]
5. Caution use with potential other herbal products with estrogen-like effects: alfalfa, burdock, hops, licorice, pomegranate, red clover, soy, thyme, white horehound and yucca[8]
6. In nature, black cohosh contains small amounts of salicylic acid, thus it may increase the anti-platelet effects of herbs such as aspen bark, birch, willow bark and wintergreen.[8] Also, theoretically caution with other herbs that may increase risk of bleeding such as ginkgo biloba, ginseng and garlic.[8]

Dose:

Preparations of black cohosh come from the roots and understems (rhizomes). (See Table 1 for examples of various available products).

The usual dose of for example, Remifemin® (a standardized extract of black cohosh) is 20 mg twice per day .

A woman can also take black cohosh in any of the following forms, three times per day:

- Powdered root or as a tea, 1-2 g
- Solid, dry 4:1 powdered extract, 250-500 mg
- Fluid extract, 1:1 tincture, 4 mg (1 tsp, or about 5 ml)[10]

Black cohosh therapy should be limited to 6 months.[3, 8, 10]

Clinical Studies of Black Cohosh

In 2001, the American College of Obstetricians and Gynecologists (ACOG) stated on the basis of consensus that black cohosh may be helpful in the short term (6 months or less) for some women with vasomotor menopausal symptoms.[6,14] Currently, black cohosh is used for menopausal symptoms including hot flashes. A few studies using various designs have been conducted to determine whether black cohosh improves menopausal symptoms but have produced conflicting data, most likely because of lack of attention to study design and short study duration (12 weeks or less). Also, there is variability in source amounts of black cohosh and outcome measures.

The HALT study which was a 12-month randomized double-blind placebo-controlled trial, involving 351 women between 45 to 55 years with at least two hot flashes and or night sweats a day compared five different therapies: 1) black cohosh; 2) A multibotanical supplement with black cohosh, alfalfa, boron, chaste tree, dong quai, false unicorn, licorice, oats , pomegranate and Siberian ginseng; 3) A multibotanical supplement plus diet counseling to increase consumption of foods containing soy; 4) Menopausal hormone therapy consisting of estrogen with or without a progestin and 5) A placebo containing no drug or supplement.[15,16] Researchers found no difference between the number of daily hot flashes and/or night sweats in any herbal supplement group when compared to placebo however the women on hormonal therapy had significantly less symptoms per day then placebo.[15,16]

For each study that shows a positive outcome with black cohosh, there is another study that supports hormone therapy or placebo as being more effective. At this point in time, there is no conclusive clinical study available and further research is needed to determine the efficacy of black cohosh for menopausal symptoms. However, clinically some women may choose to use black cohosh and their individual beneficial symptom control may outweigh the risks for these women in short-term therapy by contributing to an improved quality of life.

Other Alternative Herbal Agents that have been used in Perimenopause

Dong quai, soy, red clover, evening primrose oil and American ginseng have also been used for the management of menopausal symptoms but current data is not sufficient to support their use as single ingredient products. Dong quai, soy and red clover are used due to their similar structure to estrogen and estradiol and have a high affinity to beta-estrogen receptors which are found in the bladder, bone, heart and vasculature.[17, 18, 19] Evening primrose oil has components which are precursors to prostaglandin to reduce the menopausal symptoms of mood swings, irritability and breast tenderness.[20,21] American ginseng is thought to help with cooling effects on the body. [21] These products are frequently combined with black cohosh in multi-ingredient preparations (Table 1).

Patient Counseling Information for Black Cohosh

While black cohosh may have some positive effects for menopausal symptom control in some patients, as an herbal product it falls under the Dietary Supplement Health and Education Act of 1994. Under this act, a disclaimer in the labeling must state: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." Patients should be reminded of this disclaimer.

- Black cohosh in general is best taken at the same time every day and most manufacturers recommend giving with food.
- Duration of therapy should be limited to no more than six months.
- Women with breast cancer may want to avoid black cohosh.

Table 1. Examples of Available Herbal Products Containing Black Cohosh

Herbal Product Trade Name	Active Ingredients and strength	Suggested Dose on package	Manufacturer	Other Comments
Estroven	Vitamin E 30IU Thiamin 2mg Riboflavin 2mg Niacin 20mg Vitamin B-6 10mg Folate 400mcg Vitamin B-12 6mcg Calcium 150mg Selenium 70mcg Boron 1.5mg Estroven Calming Herbal Blend (proprietary blend of Date seed extract [Zizyphus *spinosa*] and Magnolia bark extract) 150mg Isoflavones (from Pueraria *lobata* root extract and GMO-free soybeans) 55mg Black cohosh root standardized extract 40mg	One caplet daily a few hours before bedtime with food	Amerifit Brands	Other ingredients: cellulose, croscarmellose sodium, silica, vegetable magnesium stearate, titanium dioxide (natural mineral source) vanilla and caramel color. Contains Soy.
Estroven Maximum Strength	Vitamin E 30IU Thiamin 5mg Riboflavin 5mg Niacin 20mg Vitamin B-6 20mg Folate 400mcg Vitamin B-12 25mcg Calcium 100mg Selenium 70mcg Chromium 120mcg Boron 1.5mcg Phosphorus 50mcg Cranberry juice extract 150mg Black cohosh root standardized extract 80mg Isoflavones (from Pueraria *lobata* root extract and GMO-free soybeans) 55mg Estroven Balancing Herbal Blend (proprietary blend of Green tea extract, Date seed extract [Zizyphus *spinosa*] and Magnolia bark extract) and Cimnamon twig extract 400mg	One tablet daily best taken at mealtime	Amerifit Brands	
Estroven PM	Vitamin B-12 6mcg Calcium 60mg Vitamin D 800iu Magnesium Oxide 100mg Estrogen Relaxing Botanical Blend (proprietary blend of Magnolia bark extract , Chamomile flower extract, Date seed extract [sisyphus *spinoza*] and Orange blossoms) 75mg Estrogen Herbal Sleep Blend (proprietary blend of valerian root standardized extract, passionflower whole plant extract, and Hops *strobile* standardized extract) 75mg Chaste tree berry standardized extract 75mg Black cohosh root standardized extract 80mg	Take one tablet before bedtime	Amerifit Brands	Other ingredients : microcrystallized cellulose, croscarmellose sodium, vegetable stearic acid, silica, hypromellose, vegetable magnesium stearate, hydroxypropyl cellulose, natural source polyethylene glycol, orange and vanilla extract essences, and natural color

continued

- Women who are pregnant should not use black cohosh.
- Women who have liver disease should use caution with black cohosh and liver function tests should be monitored.

Non Pharmacologic Patient Interventions for Menopausal Symptoms:

- Exercise
- Get to a healthy weight and keep it there
- Adequate sleep - go to bed and wake up are the same time each day to regulate sleep/wake cycle
- Stop smoking
- Adequate fluid intake

Table 1. Examples of Available Herbal Products Containing Black Cohosh *continued*

Estroven Energy	Vitamin E 30IU/ 1 cap Thiamin 2mg Riboflavin 2mg Niacin 20mg Vitamin B-6 10mg Folate 400mcg Vitamin B-12 6mcg Vitamin D 800iu Calcium 100mg Selenium 70mcg Boron 1.5mg Estroven Energy Blend (proprietary blend of Chinese date seed extract [Zizyphus spinosa] Green tea extract and Magnolia bark standardized extract and Yerbe mate leaves extract) 200mg Isoflavones (from Pueraria lobata root extract and GMO-free soybeans) 55mg Black cohosh root standardized extract 40mg	Take one (1) capsule every morning with food. Some women may notice benefits in 7-10 days, but since Estroven® Energy is natural, it works gradually over time. Most ongoing benefits are realized within 30 to 60 days of use.	Amerifit Brands	Other ingredients: gelatin, cellulose, croscarmellose sodium, silica, vegetable magnesium stearate, titanium dioxide (natural mineral source) vanilla and caramel color, Contains Soy.
Remifemin	Standardized to be equivalent to 20 mg black cohosh (Cimicifuga *racemosa*) root and rhizome.	Take one tablet AM + PM	Schaper & Brummer GmbH & Co. KG.	Other Ingredients: Lactose (milk), cellulose, potato starch, magnesium stearate, and natural peppermint flavor.
Remifemin Good Night	Standardized to be equivalent to 40 mg black cohosh (Cimicifuga *racemosa*) root and rhizome.(RemiSure) valerian (Valeriana *officinalis*) root extract 4:1 lemon balm (Melissa *officinalis*) leaf extract 4:1, hops (Humulus *lupulus*) strobile extract 4:1 equivalent to 286mg	Take one tablet at bedtime with water – may be increased to two tablets	Schaper & Brummer GmbH & Co. KG.	Other ingredients : cellulose, modified cellulose, maltodextrin, magenesium stearate, silicon dioxide, titanium dioxide color, soy lecithin, spirulina color, and carnauba wax.
EstroSoy™ Plus	Vitamin C 1.5mg/2 cap Fermented Soy, dried 6.0% extract (bean) (containing 40 mg total isoflavones) 670mg /2 cap Red Clover (stern, leaf, flower) 360mg /2 cap Standardized Black Cohosh, dried 2.5% extract (root, rhizome) (containing 1 mg triterpene glycosides) vitamin B1 (as Thiamin Mononitrate) 40mg /2 cap	Take 2 capsules daily with water	Nature's Way	Other ingredients: Gelatin, Magnesium stearate

continued

Some specific behavioral interventions for hot flashes can include:

- Wear layered cotton clothing
- Avoid coffee, alcohol, spicy foods
- Avoid or reduce stress!
- Sip cool drinks or use ice packs or cool compress.
- Relaxation and deep breathing (6-8 breaths per minute) several times a day
- Eliminate hot baths or showers before bedtime
- Exercise
- Acupuncture and/or Yoga – can be helpful for some women

Conclusion

Review of the literature shows conflicting evidence of efficacy for black cohosh. Many studies of menopausal symptoms have significant placebo effects so it is difficult to tell the true value of hormonal therapy or any alternative therapies. For some women black cohosh may have some positive effects on menopausal symptoms and improvement their quality of life significantly. For other women, black cohosh may have no effects at all or have uncomfortable side effects or contribute to long term complications. In conclusion, the current data is not conclusive as to the efficacy of black cohosh in menopausal symptom control and more rigorous scientific studies should be conducted.

About the Authors

Janice Hoffman, Pham.. D. is currently an Assistant Professor of Pharmacy Practice and Administration at WesternU and is developing a clinical practice site in geriatrics. Dr. Hoffman has nothing to disclose or any biases.

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Table 1. Examples of Available Herbal Products Containing Black Cohosh *continued*

Change –O- Life 440mg	Proprietary Blend: black cohosh root, sarsaparilla root, siberian Eleuthero root , Licorice root, Blessed Thistle (stem, leaf, flower), Dong Quai root, Pomegranate seed 1.32g/3 caps.	Take 3 capsules three times daily, preferably with food.	Nature's Way	Other ingredients: Gelatin (capsule), magnesium stearate
Black Cohosh Root with Licorice and Don Quai 80mg	Black Cohosh (Cimicifuga racemosa) (root) [Standardized to contain 2.5% total Triterpene Glycosides, calculated as 27-Deoxyactein (4 mg)] 160mg /2 cap Licorice (Glycyrrhiza *glabra*) (root) 250mg/2 cap Dong Quai (Angelica *sinensis*) (root) 250mg /2cap	Take 2 capsules daily, preferably at separate times (1 in the morning, 1 in the evening).	Now Foods	Other ingredients: Gelatin (capsule), Rice Flour and Magnesium Stearate (vegetable source). Contains no milk, wheat, gluten, corn, yeast, sugar, salt or soy.
Red Clover/Black Cohosh 225mg/40mg	Red Clover Extract(Trifolium *pratense*)(Flower) (min. 18% Total Isoflavones) (Standardized Extract) (yields 40 mg total isoflavones) 225 per 1 Vcap black cohosh Extract(Cimicifuga *racemosa*) (Root) (min. 2.5% Triterpene Glycosides)(Standardized Extract) 40mg per 1 Vcap	Take 1 Vcap 1-2 times daily.	Now Foods	Other ingredients: Cellulose (capsule), White Rice Flour, Silica and Magnesium Stearate (vegetable source). Contains no sugar, salt, yeast, wheat, gluten, soy, milk, egg, or preservatives.
Black Cohosh Extract 40mg	Black cohosh (Cimicifuga racemosa), powdered extract 1:1 (root & rhizome) 40mg/cap Triterpene glycosides (2.5%, calculated as 27-deoxyactein) 1mg/cap	1 capsule, 1- 2 times per day preferably before meals or as directed by a health care professional.	Natural Factors	Other ingredients: Cellulose, gelatin capsule (gelatin, purified water), magnesium stearate (vegetable grade). Contains no artificial preservatives, color or sweeteners; no corn, dairy, wheat or yeast.
Hot Flash	Calcium 134mg/ 3 tabs Genistein-Rich Soy Concentrate (SoyLife™) 2.1g/3tabs (Yielding 63 mg Total Isoflavones) black cohosh Root Standardized Extract 2.5% 160mg/3 tab (Yielding 4 mg Triterpene Glycosides (containing 27-deoxyactein) Dong Quai Root Extract (4:1) 150mg/3 tabs Licorice Root Extract (4:1) 150mg/3 tabs Chaste Tree Berry Extract (10:1) 100mg/3 tabs	3 tablets daily, or as recommended by your health care professional. For best results, use this product for at least 4 weeks	Source Naturals	Other ingredients: Dibasic calcium phosphate, sorbitol, stearic acid, colloidal silicon dioxide, modified cellulose gum, and magnesium stearate. Contains wheat/gluten and soy. Suitable for vegetarians. Contains no yeast, dairy, or egg. Contains no sugar, preservatives or artificial color, flavor or fragrance

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