

NCCAM Director's Report

Promise in Research on Complementary and Alternative Medicine

*Advisory Committee to the Director
National Institutes of Health
December 5, 2008*



Legislative language

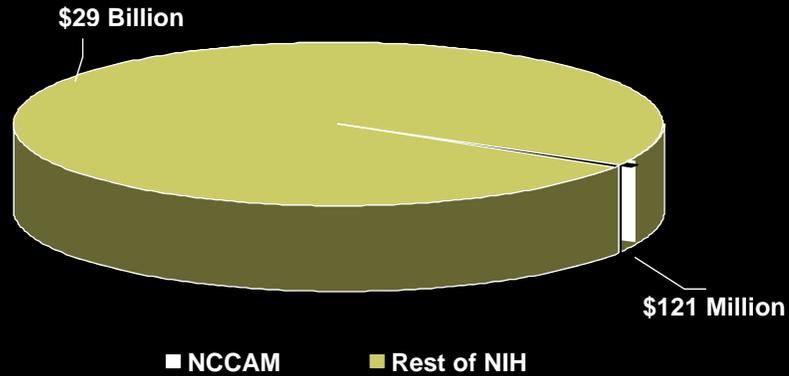
“The general purposes of the National Center for Complementary and Alternative Medicine (NCCAM) are the conduct and support of basic and applied research...research training, and other programs with respect to identifying, investigating, and validating complementary and alternative treatment, diagnostic, and prevention modalities, disciplines and systems.”

P.L. 105-277

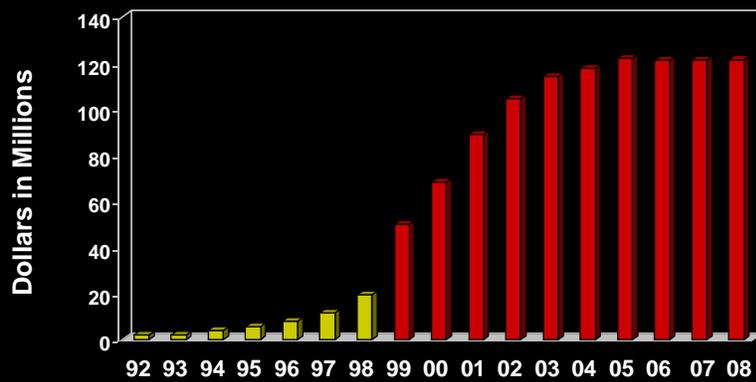
October 1998



NCCAM's Budget: 0.4% of the NIH Total



NCCAM's Appropriations History



Our Mission

- Explore complementary and alternative healing practices *using rigorous scientific methods* and develop the evidence base for safety and efficacy of CAM approaches
- Support the development of the research community of CAM researchers
- Disseminate authoritative information about CAM to the public and professionals



Topics:

- Patterns of CAM use by the American public
- Achievements to date – and areas of promise
 - Natural product research at NCCAM
 - Research on mind and body CAM practices
- Lessons learned, and looking forward



NHIS CAM Modules: 2002 and 2007



- 2007 Survey: 36 different CAM therapies for 81 different diseases/conditions
- Sample of 23,000 adults

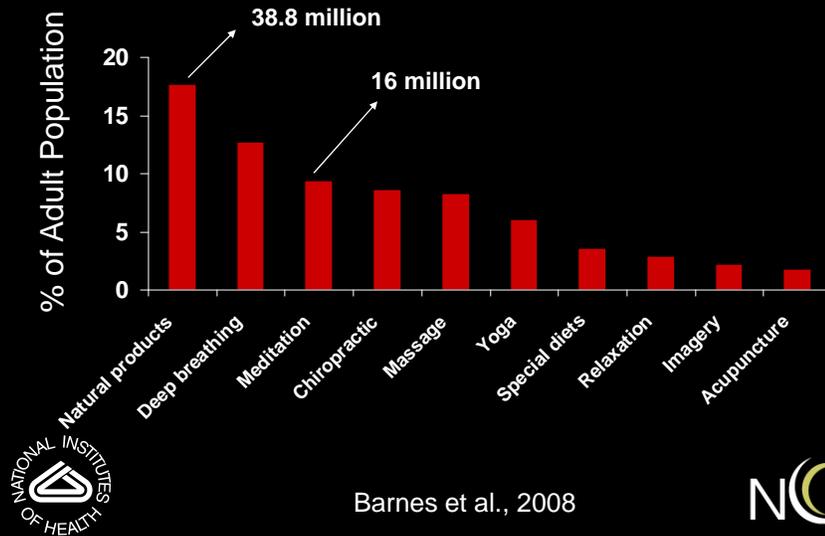


NHIS CAM Module Survey: Demographics of CAM Use, 2007

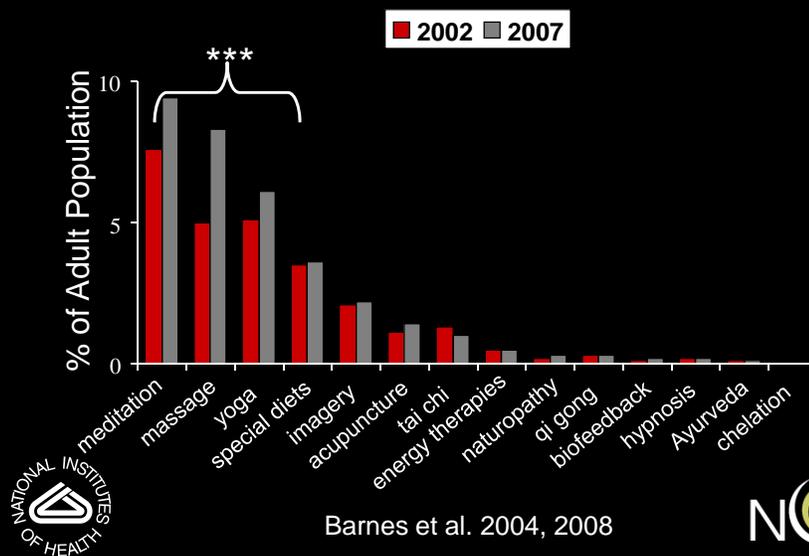
- Approx 40% of American public use CAM, consistent with earlier surveys
- Widespread in all demographic groups
- Women > men
- West >Midwest >Northeast >South
- Greater use in people with higher education levels



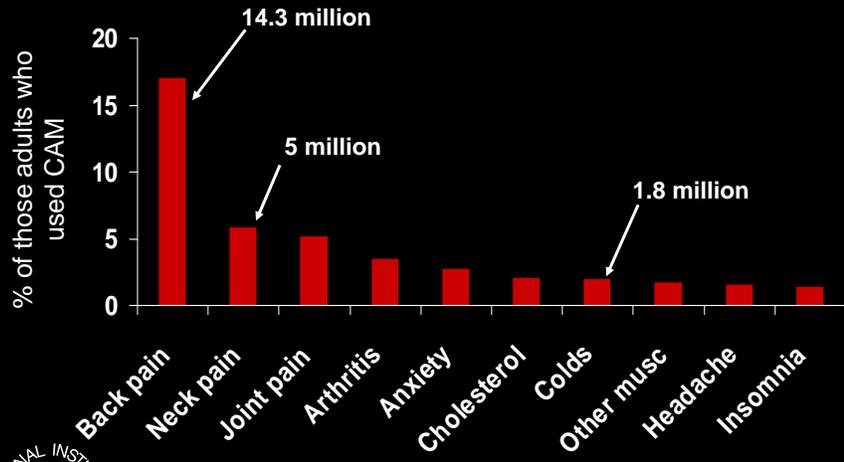
Adult Use of Selected CAM Therapies: United States, 2007



Adult Use of Selected CAM Therapies: 2002 vs. 2007



Adult Use of CAM for Selected Conditions: 2007

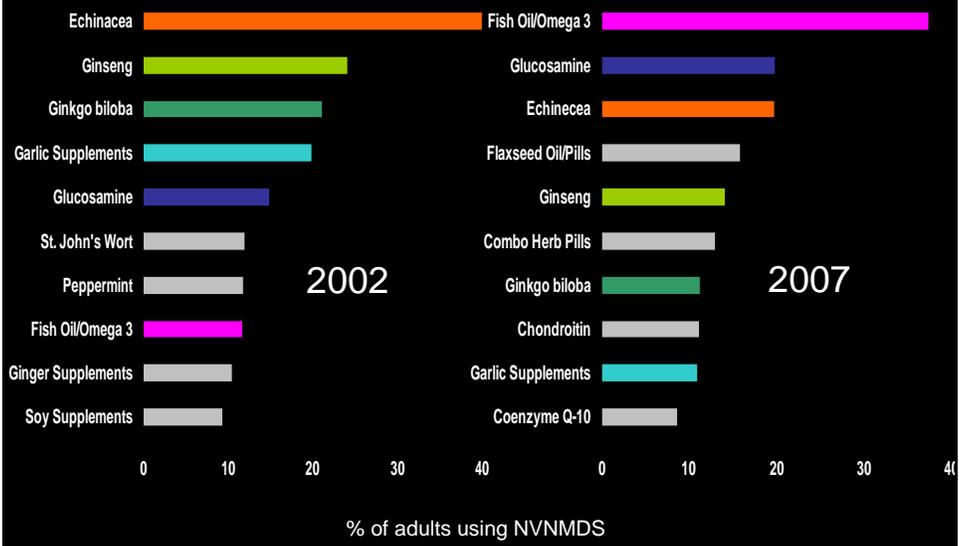


Barnes et al., 2008

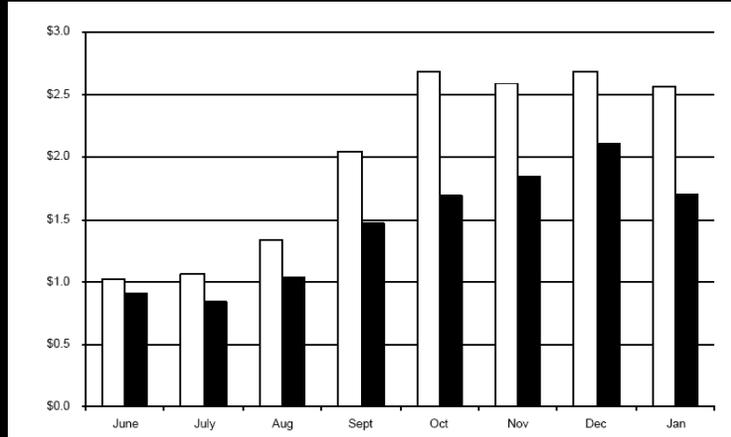


Top Herbal Medicines and Other NVNMDS:

NVNMDS = non-vitamin/non-mineral dietary supplements



Echinacea Sales; 4-Week Periods: 2004 vs. 2005.
NEJM Echinacea study – published July 2005



Source: Nutrition Business Journal 2006



The New York Times
 Ginkgo Biloba Ineffective Against Dementia,
 Researchers Find

By SCOTT CAHILL
 Published November 19, 2009

The largest and longest independent clinical trial to assess ginkgo biloba's ability to prevent memory loss has found that the supplement does not prevent or delay dementia or Alzheimer's disease, researchers are reporting.

The study is the first trial large enough to accurately assess the plant extract's effect on the incidence of dementia, experts said, and the results dashed hopes that it is an effective preventative. In fact, there were more cases of dementia among participants who were taking ginkgo biloba than among those who were taking a placebo, though the difference was not statistically significant.

"We were disappointed," said Dr. Steven T. DeKosky, dean of the School of Medicine at the University of Virginia and the principal investigator. "We were hopeful this would work."

U.S. News & World Report
 Health Buzz: New Study Casts Further Doubt on
 Popular Osteoarthritis Supplements

January 16, 2010
 October 1, 2009

The popular supplements glucosamine and chondroitin sulfate don't appear to work any better than placebo in slowing down the loss of knee cartilage in osteoarthritis patients, Reuters wire one and published this month in the journal *Arthritis & Rheumatism*. In a previous study, researchers also cast doubt on the effectiveness of the supplements, though researchers said more study is needed to confirm this week's findings.

"The study actually says more about what we need to do for the next investigation than for what patients should do," researcher Allen Sawitzke, an associate professor of internal medicine at the University of Utah School of Medicine, said HealthDay.

A recent study found that arthroscopic surgery for knee osteoarthritis doesn't work any better than physical therapy and medications, U.S. News's Adam Voiland provided a list of six alternatives to arthroscopic knee surgery. Earlier, Katherine Holton encouraged patients to listen to their knees.



What do the numbers tell us?

- Complementary and alternative health practices, especially natural products, meditation, massage, manipulative therapies, and yoga are widely used by the American public
- Chronic pain, especially back pain, is the most common reason
- Media coverage and public interest is strong
- Data on natural product use from both NHIS and industry sources indicates significant public impact of research results



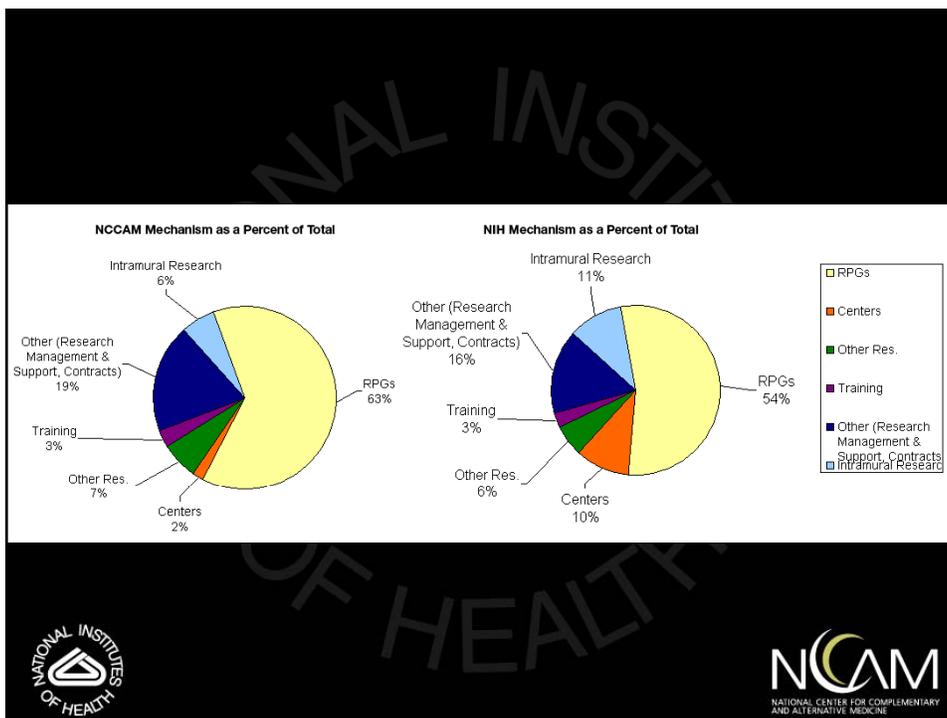
Cheat death.

The antioxidant power of
pomegranate juice:



Achievements: 9 years of natural product research at NCCAM

- Implementation, in partnership with other IC's, of 6 major high-quality RCT's of widely used natural products
- Rigorous processes to assess quality and consistency of herbal and other natural products used in NCCAM research
(PIWG: Product Integrity Working Group)
- A strong portfolio of investigator-initiated research on plant-derived natural products, vitamins, and probiotics



Examples: Areas of promise in natural product research at NCCAM

- Insight into molecular targets of dietary small molecules such as quercetins, curcumin, other polyphenols and flavenoids
- CoQ-10 for statin myopathy
- Anti-inflammatory actions of omega 3 FA's at clinically relevant concentrations
- Clarification of potential cranberry juice mechanism: effect on bacterial adherence
- Effects of pre- and probiotics on the human microbiome
- Collaborative study of active components of traditional Chinese herbal remedies



Nature Chemical Biology, July 2007

COMMENTARY

Revisiting the ancient concept of botanical therapeutics

Barbara M Schmidt, David M Ribnick, Peter E Lipsky & Ilya Raskin

Mixtures of interacting compounds produced by plants may provide important combination therapies that simultaneously affect multiple pharmacological targets and provide clinical efficacy beyond the reach of single compound-based drugs. Developing innovative scientific methods for discovery, validation, characterization and standardization of these

to their acceptance into mainstream medicine.



Figure 2 Thungergod vine and its natural products. (a) Thungergod vine *Tripterygium wilfordii* grown hydroponically. (b) Structures of the diterpenoids triptolidide and triptolide, two active components in Thungergod vine.

Autismunity Branch, National Institutes of Health, 3000 Rockville Pike, Bethesda, Maryland 20892, USA. e-mail: raskin@AESOR.Rogers.edu

being either a natural product or a mixture thereof. Only one drug or compound combination could be completely *de novo* combinatorial. The above analysis does not include vaccines which are by definition non-natural.

It is noted that 29% of all drugs presently come from plants.¹⁴ This ratio that plant-derived drugs make a significant segment of natural product-natural chemicals. Out of many families of metabolites, or compounds on growth of a plant is not dependent on co-occurring alkaloids have a pharmacology, ranging in effects: anticholinergics (atropine) to analgesics (alkaloids) and from antiparasitics (anticholinergetics (galantamine) (placenta (vinblastine/vincristine))¹⁵ to as plentiful as alkaloids in the same species, terpenoids (including) have made an equally important contribution to human health. They range from K⁺ pump-inhibiting cardiac glycosides (Digitalis spp. (recognized as a for congestive heart failure by Linnaeus in 1753); to anticancer (Taxol, isolated from the Pacific by Monroe E. Wall and Mansukh Chatterjee in 1962)¹⁶ to anti-inflam-

Flenolics (mostly phenylpropanoids) contributed aspirin and podophyllotoxin to modern medicine. Figure 1 summarizes the most important structural classes of pharmacologically active secondary metabolites from plants. It is important to note, however, that the activity of some natural products has yet to be certified by extensive testing or clinical trials; we anticipate that these cases will benefit from the same rigorous attention as those described below for multicomponent botanical therapeutics (MCTBs).

This overrepresentation of natural product-derived drugs begs the question of whether plant secondary metabolites and related synthetic compounds perform better as drugs than randomly synthesized compounds. Plant natural products, enzymes, receptors and regulatory proteins have common evolutionary roots, originating from a small number of parent molecules. These parent molecules were present in primitive life forms and therefore co-evolved to interact with one another. Although their functions and structures have subsequently diverged, some structural kinship still remains that makes natural products, on average, better ligands for human clinical targets than randomly synthesized compounds. As one example of functional conservation between secondary metabolites, the animal eye pigments lutein and zeaxanthin, which protect the eye from harmful short wave radiation, are the same molecules that protect plant photosynthetic machinery from oxidative damage¹⁷. These carotenoids probably evolved from a common biochemical ancestor playing a primordial role in cellular photochemistry. However, animals have lost the ability to make these compounds and now need

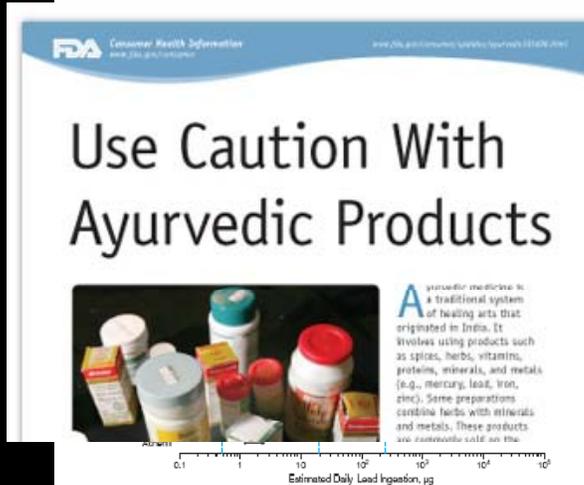


JAMA
August 27, 2008

Lead, Mercury, and Arsenic in US- and Indian-Manufactured Ayurvedic Medicines Sold via the Internet

Robert B. Saper, MD, MPH
Russell S. Phillips, MD
Anusha Sehgal, MD(Ayurveda)

Context Lead, mercury, and arsenic have been detected in a substantial proportion of Indian-manufactured traditional Ayurvedic medicines. Metals may be present due to the practice of rasa shastra (combining herbs with metals, minerals, and gems). Whether toxic metals are present in both US- and Indian-manufactured Ayurvedic medi-



... Ayurvedic medicines available via the Internet. The authors measured the lead, mercury, and arsenic and to compare the prevalence of these metals in Indian-manufactured Ayurvedic medicines and between rasa sha-

... is and the search terms Ayurveda and Ayurvedic. The authors also compared the prevalence of these metals in Indian-manufactured Ayurvedic herbs, for-



Achievements: 9 years of research on mind and body CAM approaches

- Rigorous scientific methods from behavioral science and modern neuroscience applied to meditation, acupuncture, and other mind-body interventions

BMJ

RESEARCH

Prescribing "placebo treatments": results of national survey of US internists and rheumatologists

Jon C. Tilburt, staff scientist,¹ Ezekiel J. Emanuel, director,¹ Ted J. Kaptchuk, associate director,² Farr A. Curlin, assistant professor of medicine,³ Franklin G. Miller, director, research ethics programme¹



Examples: Areas of promise in research on mind and body CAM approaches

- Benefits of yoga and Tai chi for balance and avoiding falls in elderly people
- Insight into of central mechanisms of placebo analgesia
- Contribution of acupuncture and other mind and body practices to pain management



Annals of Internal Medicine

ARTICLE

Comparing Yoga, Exercise, and a Self-Care Book for Chronic Low Back Pain

A Randomized, Controlled Trial

Karen J. Sherman, PhD, MPH; Daniel C. Cherkin, PhD; Janet Erro, RN, MN, PNP; Diana L. Miglioretti, PhD; and Richard A. Deyo, MD, MPH

LITERATURE REVIEW

Journal of Manipulative and Physiological Therapeutics

UNLOADED MOVEMENT FACILITATION EXERCISE COMPARED TO NO EXERCISE OR ALTERNATIVE THERAPY ON OUTCOMES FOR PEOPLE WITH NONSPECIFIC CHRONIC LOW BACK PAIN: A SYSTEMATIC REVIEW

Susan C. Slade, PT,* and Jennifer L. Keating, PhD, PT^b

CLINICAL GUIDELINES

Annals of Internal Medicine

Nonpharmacologic Therapies for Acute and Chronic Low Back Pain: A Review of the Evidence for an American Pain Society/American College of Physicians Clinical Practice Guideline

Roger Chou, MD, and Laurie Hoyt Huffman, MS



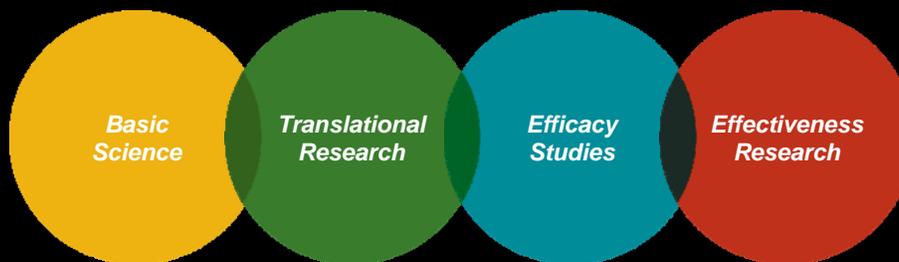
Current Initiative: Non-pharmacological Management of Back Pain

What strategies to improve the management of back pain are ready for rigorous testing?

What is the 'real world' effectiveness of CAM modalities such as manipulation, manual therapies, acupuncture, and mind-body approaches?



Lessons learned



What we would like to have before another major RCT of a natural product:

- Strong biological hypothesis
- Good chemistry (ADME)
- Marker(s) to verify biological effect *in vivo*
- Maximally sensitive outcome measures and trial design
- 'Proof of concept' preliminary clinical data
- Characterized target population



Challenges:

- NCCAM covers a broad range of science and needs access to expertise in a broad range of scientific and clinical disciplines
- Methodologies to explore CAM approaches are in many areas not mature
- NCCAM has a broad range of diverse constituencies
- NCCAM bridges diverse worlds



Input

- NCCAM Advisory Council
- NCCAM Stakeholders
- NIH 'in house' expertise
- Academic and private sector expertise



10 Year - Strategic Planning

Intramural Strategic Review Panel

Michael Irwin, MD, UCLA *Chair*

Nancy Adler, PhD, UCSF (*ACD liaison*)

Stephen Barnes, PhD, UAB (*NCCAM Council liaison*)

Tommy Cheng, PhD, Yale

William Kelly, MD, University of Penn

Story Landis, PhD, Director NINDS, Former NINDS SD

Tieraona Low Dog, MD, University of Arizona (*BSC liaison*)

Max Muenke, MD, PhD, NHGRI



Acknowledgements

- NHIS CAM Survey
 - Richard Nahin, NCCAM
 - Patricia Barnes, NCHS/CDC



National Center for Complementary
and Alternative Medicine

1.888.644.6226
nccam.nih.gov



What is the question?

How does
it work?

Can it be
studied in
people?

What are the
specific
effects?

Is it a
good
treatment?

