

Herbal Dietary Supplement Special Interest Group, AACT

Jan. 2015 Abstracts

1. Dietary supplements: sorting out the science. A few supplements show limited, possible benefits for people with heart disease. But some popular ones don't--and others may be dangerous. Harv Heart Lett. 2014 Aug;24(12):1, 7. PubMed PMID: 25230415.

A lay summary of the April NEJM (2014;370(14):1277-) article by Pieter Cohen.

2. Zabłocka-Słowińska K, Jawna K, Grajeta H, Biernat J. Interactions between preparations containing female sex hormones and dietary supplements. Adv Clin Exp Med. 2014 Jul-Aug;23(4):657-63. Review. PubMed PMID: 25166453.

Abstract

An increasing number of premenopausal women use contraception whereas postmenopausal women use hormone replacement therapy (HRT). This long-term hormone therapy poses a high risk of interactions with dietary supplements. Taking estrogens at the same time as selective estrogen receptor modulators (SERMs), biologically-active compounds of glycine soja, *Ginkgo biloba* or *Pimpinella anisum*, may distort the final effect of the hormone agent. On the other hand, estrogen therapy coupled with melatonin or retinol supplementation may lead to an increased level of dietary supplements in the serum as studies have proved a concomitant beneficial effect of HRT and vitamin E supplementation on lipid profiles. In turn, taking preparations containing St John's wort during hormone therapy may lead to a reduction in hormone concentrations in serum and debilitation of the pharmacological effect. It results from the inductive effect of the biologically-active compounds of St John's wort on the metabolism of hormones as a result of the enhanced activity of cytochrome P450 CYP3A4

3. Fish oil supplements. JAMA. 2014 Aug 27;312(8):839-40. doi: 10.1001/jama.2014.9758. PubMed PMID: 25157728.

One page summary document from The Medical Letter on Drugs and Therapeutics

4. Edakkanambeth Varayil J, Bauer BA, Hurt RT. Over-the-counter enzyme supplements: what a clinician needs to know. Mayo Clin Proc. 2014 Sep;89(9):1307-12. doi: 10.1016/j.mayocp.2014.05.015. Epub 2014 Aug 4. Review. PubMed PMID: 25103998.

Abstract

Over-the-counter (OTC) enzyme use is increasing in frequency in the United States. The numerous health benefit claims by manufacturers are leading to a surge in enzyme use for various conditions and symptoms. Clinicians need to help patients navigate this

complex realm and make informed decisions about the use of OTC enzymes. This review focuses on key concepts for health care providers to understand the current evidence, risks, and benefits of OTC enzymes.

5. Shike M, Doane AS, Russo L, Cabal R, Reis-Filo J, Gerald W, Cody H, Khanin R, Bromberg J, Norton L. The effects of soy supplementation on gene expression in breast cancer: a randomized placebo-controlled study. *J Natl Cancer Inst.* 2014 Sep 4;106(9). pii: dju189. doi: 10.1093/jnci/dju189. Print 2014 Sep. PubMed PMID: 25190728.

Background There are conflicting reports on the impact of soy on breast carcinogenesis. This study examines the effects of soy supplementation on breast cancer-related genes and pathways. **Methods** Women (n = 140) with early-stage breast cancer were randomly assigned to soy protein supplementation (n = 70) or placebo (n = 70) for 7 to 30 days, from diagnosis until surgery. Adherence was determined by plasma isoflavones: genistein and daidzein. Gene expression changes were evaluated by NanoString in pre- and posttreatment tumor tissue. Genome-wide expression analysis was performed on posttreatment tissue. Proliferation (Ki67) and apoptosis (Cas3) were assessed by immunohistochemistry. **Results** Plasma isoflavones rose in the soy group (two-sided Wilcoxon rank-sum test, $P < .001$) and did not change in the placebo group. In paired analysis of pre- and posttreatment samples, 21 genes (out of 202) showed altered expression (two-sided Student's t-test, $P < .05$). Several genes including FANCC and UGT2A1 revealed different magnitude and direction of expression changes between the two groups (two-sided Student's t-test, $P < .05$). A high-genistein signature consisting of 126 differentially expressed genes was identified from microarray analysis of tumors. This signature was characterized by overexpression (>2 -fold) of cell cycle transcripts, including those that promote cell proliferation, such as FGFR2, E2F5, BUB1, CCNB2, MYBL2, CDK1, and CDC20 ($P < .01$). Soy intake did not result in statistically significant changes in Ki67 or Cas3. **Conclusions** Gene expression associated with soy intake and high plasma genistein defines a signature characterized by overexpression of FGFR2 and genes that drive cell cycle and proliferation pathways. These findings raise the concerns that in a subset of women soy could adversely affect gene expression in breast cancer.

6. Jordan VC. Avoiding the bad and enhancing the good of soy supplements in breast cancer. *J Natl Cancer Inst.* 2014 Sep 4;106(9). pii: dju233. doi: 10.1093/jnci/dju233. Print 2014 Sep. PubMed PMID: 25190729.

Editorial on accompanying article by Shike M et al. (#5)

7. Zhang HW, Lin ZX, Xu C, Leung C, Chan LS. Astragalus (a traditional Chinese medicine) for treating chronic kidney disease. *Cochrane Database Syst Rev.* 2014 Oct 22;10:CD008369. doi: 10.1002/14651858.CD008369.pub2. Review. PubMed PMID: 25335553.

Summary: Chronic kidney disease affects increasing numbers of people around the world, but as yet, effective strategies to control its progression have not been universally accepted. Astragalus is one of most widely used herbs for treating kidney disease. We conducted this review to evaluate the benefits and potential harms of Astragalus for the treatment of people with chronic kidney disease. We searched the literature published up to July 2014 and summarised 22 studies involving 1323 people with chronic kidney disease, including both on dialysis treatment or not. Although we found some promising evidence suggesting that when given with conventional treatment, Astragalus may help to decrease the serum creatinine, reduce the amount of protein lost in urine and diminish the effects of some complications, such as anaemia and malnutrition, evidence quality was low. We found that errors and omissions in study methods and reporting were likely to have flawed results among the studies we assessed. Possible adverse effects associated with Astragalus injection should be noted, although we found no relevant reports from included studies.

8. Qiu F, McAlpine JB, Krause EC, Chen SN, Pauli GE. Pharmacognosy of black cohosh: the phytochemical and biological profile of a major botanical dietary supplement. *Prog Chem Org Nat Prod*. 2014;99:1-68. Review. PubMed PMID: 25296437.

Abstract

The ethnobotanical, Black Cohosh, a preparation from the roots/rhizomes of *Actaea racemosa*, has been the subject of extensive investigations. Despite the fact that sales figures place it among the top ten U.S. dietary supplements, the mechanisms of its amelioration of the adverse effects of menstruation and menopause remain largely undefined. The plant is a prodigious “factory” of complex secondary metabolites, with almost 50 cycloartane triterpenes, over 70 alkaloids, and 11 phenolic acids characterized so far, and this chapter discusses the chemistry of the *A. racemosa* secondary metabolome in detail. While numerous in vitro and in vivo pharmacological and biological studies attribute diverse specific biochemical effects to individual metabolites or defined extracts, an adequate explanation of potencies and drug(-like) concentrations is still lacking. As many of the effects may play a role in the alleviation of menopausal symptoms, the possibility exists that the overall effect may be the result of a combination of both multiple bioactive principles and several synergistic interactions. On careful analysis, a purported hepatotoxicity risk raised has been relegated to “a possible rare idiosyncratic reaction”. More than 50 clinical studies defy definitive analysis, other than confirming that the material is safe, in part because of poor study design and differences in preparations used. The global literature on Black Cohosh is almost unanimous in a call for larger, more well-designed clinical studies, and recent advances in the understanding of the phytoconstituents justify a more thorough secondary metabolomics analysis of this interesting North American plant.

9. Milić N, Milosević N, Golocorbin Kon S, Bozić T, Abenavoli L, Borrelli F. Warfarin interactions with medicinal herbs. *Nat Prod Commun*. 2014 Aug;9(8):1211-6. Review. PubMed PMID: 25233607.

Abstract

Recognition of the adverse effects of medicinal herbs is not routine and the reports on such effects are even less frequent in clinical practice. Potential herb-drug interactions are of a major safety concern, especially for drugs with narrow therapeutic indices like warfarin, which can lead to severe adverse reactions that are sometimes life-threatening. The interactions between warfarin and medicinal herbs described in the literature have been summarized in this paper relying on Medline database (via PubMed) using the key words: warfarin, herbal supplements and interactions. The references on the analyzed literature have been investigated in order to collect the existing data. The case reports with severe adverse effects such as spontaneous postoperative bleeding, formation of hematomas, hematemesis, melena, thrombosis, subarachnoid hemorrhage and/or subdural hematomas after concomitant use of warfarin and the medicinal herbs: *Panax ginseng*, *Hypericum perforatum*, *Salvia miltiorizza*, *Gingko biloba*, *Serenoa repens*, *Angelica sinensis*, *Vaccinium* species, *Allium sativum*, *Zingiber officinale*, *Tanacetum parthenium*, *Lucium barbarum*, *Matricaria chamomilla*, *Boswellia serrata* and *Camellia sinensis* have been estimated. Some of the interactions between warfarin and medicinal herbs have been well assessed proving that they are closely-dependent. The interactions between warfarin and medicinal herbs, not generally reported in previous reviews, are presented in our review. The health professionals who are involved in treating the patients are expected to be fully informed about the interactions between warfarin and medicinal herbs in order to minimize the health risks of the patients.

10. Khurana A, Dasanu CA. Hepatitis associated aplastic anemia: case report and discussion. Conn Med. 2014 Sep;78(8):493-5. PubMed PMID: 25314890.

Abstract

Aplastic anemia (AA) is thought to represent an autoimmune disorder leading to generation of activated CD8+ T-cells that target the bone marrow precursors. Hepatitis associated aplastic anemia (HAAA) is a subtype of aplastic anemia that develops within several months of an episode of acute hepatitis. Etiologic agents include hepatitis viruses (A-E and G), Epstein-Bar virus, cytomegalovirus, HIV, parvovirus B19, and echoviruses amongst others. However, most HAAA cases are labeled "idiopathic" as the inciting agent cannot be identified. Drugs and/or toxins are rarely causal factors. We describe herein a unique case of HAAA linked with the anabolic steroid methasterone that caused a transient cholestatic hepatitis and, subsequently, a severe aplastic anemia in a young man.

11. de Souza Silva JE, Santos Souza CA, da Silva TB, Gomes IA, Brito Gde C, de Souza Araújo AA, de Lyra-Júnior DP, da Silva WB, da Silva FA. Use of herbal medicines by elderly patients: A systematic review. Arch Gerontol Geriatr. 2014 Sep-Oct;59(2):227-33. doi: 10.1016/j.archger.2014.06.002. Epub 2014 Jul 9. Review. PubMed PMID: 25063588.

Abstract

Objectives We aimed to survey the published literature for articles that describe the use of herbal supplements by elderly patients and to summarize important aspects of selected studies, including most commonly used supplements, study type, study location, and potential hazards of herbal supplement use. **Methods** Literature searches were conducted on three scientific/medical databases: Medline, Web of Science, and Scopus. Search results were examined for articles involving the use of herbal products in the elderly population that met selection criteria. **Results** Initial searches yielded 1297 articles. Of these original results, only 16 met specific selection criteria. Twelve (75%) of studies identified were performed in North America. Nine studies (56.25%) were conducted in the United States. Seven of the studies were cross-sectional (43.8%). The most commonly reported were ginkgo biloba, garlic, ginseng, aloe vera, chamomile, spearmint, and ginger. Of these, ginkgo and garlic are the most commonly used among community-dwelling elderly. Both of these supplements have the potential to interact with anticoagulants and produce bruising or bleeding problems. **Conclusions** The use of herbal supplements is common among the elderly, a population that takes a disproportionate share of prescription medications compared to that taken by younger populations. Among the problems uncovered by these studies was a lack of dialog between medical professionals and patients about the use of herbal supplements. Prescribers need to consider the use of herbal supplements and discuss the matter with their elderly patients when making decisions about pharmacological treatments.

12. Smeriglio A, Tomaino A, Trombetta D. Herbal products in pregnancy: experimental studies and clinical reports. *Phytother Res.* 2014 Aug;28(8):1107-16. doi: 10.1002/ptr.5106. Epub 2014 Jan 7. Review. PubMed PMID: 24399745.

The aim of this work is to provide an update from an overview of the literature of the most frequently consumed herbal remedies during pregnancy, both alone and concomitantly with prescribed medications and particularly on their side effects to the mother and fetus. We have also analyzed some of the adverse interactions that may occur due to concomitant use of herbal and pharmaceutical products during pregnancy. Herbal remedies are not evaluated according to the same standards as pharmaceuticals, and in the USA some of it are not licensed but sold as food supplements. There is a lack of basic knowledge on the part of both clinicians and patients as to the indications for use and safety of herbal medicines used in pregnancy and lactation. If 'traditional use' is the only available information, the pregnant woman should be made aware of this to enable her to make an informed decision concerning potential use.