

## Safety and Efficacy of Top 20 Herbs and Supplements Used by Children and Teens

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### • Faculty Disclosure Information

- In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in my presentation.
- This presentation will include discussion of pharmaceuticals that have not been approved by the FDA

## Objectives

- This session will provide an overview of herbal medication usage patterns and discuss the most commonly used herb and supplements.
- Faculty will provide an update on the top 10 herbs and supplements used by children and adolescents, including Arnica, Butterbur, creatine, kava, probiotics, and St. John's wort.
- Emphasis will be placed on the efficacy and safety of herbal medicines. Resources will be shared, including information on how to receive updates on herbal medicines and supplements.

## 2012 National Health Interview Survey (NHIS)

- 11.6 percent of the more than 10,000 children aged 4 to 17 included in the survey had used or been given some form of complementary health product or practice during the past year.
- The most frequently used complementary approaches for children were natural products such as fish oil, melatonin, or probiotics and chiropractic or osteopathic manipulation.
- For children, complementary approaches were most often used for back or neck pain, other musculoskeletal conditions, head or chest colds, anxiety or stress, attention-deficit hyperactivity disorder (ADHD), and insomnia or trouble sleeping.
- CAM users were more likely than non-CAM users to be: adolescents rather than infants or; live in the West, Northeast, or Midwest compared to the South; more likely to have a parent with a college education and more likely to use prescription medication.
- Use of CAM by a parent was strongly associated with the child's use of CAM.

## Regulation: DEFINITION OF DSHEA 1994

Sec. 201(ff) The term dietary supplement --  
(1) means a product (other than tobacco) intended to supplement the diet that bears or contains any of the following dietary ingredients:  
(A) a vitamin  
(B) a mineral  
(C) an herb or other botanical  
(D) an amino acid  
(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake;  
(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)

## What the law allows:

- Products can go on the market with no testing of efficacy.
- Companies do not have to prove that their products are safe only reasonable assurance.
- Supplements do not have to be manufactured according to any standards (the reputable manufacturers are in favor of standards).
- FDA approval is not needed for package or marketing claims.

## Safety Messaging

- Raynor DK. Buyer beware? Does the information provided with herbal products available over the counter enable safe use? *BMC Med.* 2011
- 51 (75%) of 68 products contained none of the key safety messages.
- This included 4 of 12 St John's wort products, 12 of 12 ginkgo products, 6 of 7 Asian ginseng products, 20 of 21 garlic products and 9 of 13 echinacea products.
- The two products purchased that are registered under the new European Union regulations (for St John's wort) contained at least 85% of the safety messages.

## Herb Drug Interactions

- Gilmour J, Harrison C, Asadi L, Cohen MH, Vohra S. Natural health product-drug interactions: evolving responsibilities to take complementary and alternative medicine into account. *Pediatrics* 2011;128 (suppl 4):S155-S160
- Losier A, Taylor B, Fernandez CV. Use of alternative therapies by patients presenting to a pediatric emergency department. *Journal of Emergency Medicine* 2005;28:267-71.
- Posadzki P, Watson LK, Ernst E. Adverse effects of herbal medicines: an overview of systematic reviews. *Clin Med* 2013;13:7-12.

## Herbal Use in Patients Undergoing Surgery

- Approximately 26% of patients scheduled for surgery use herbal products
  - Cardiovascular instability
  - Prolongation of anesthesia/sedation
  - Bleeding
  - Electrolyte disturbances
  - Immunosuppression

Anaesthesia 2002;57:889-99

## Labeling and Manufacturing Standards Proposal

- Current good manufacturing practices (CGMPs)-manufacturing, packaging and holding standards
- Manufacturers required to evaluate the identity, purity, quality, strength and composition of their dietary ingredients and dietary supplements
- Required to report impurities, potency errors

## United States Pharmacopeia (USP) Dietary Supplement Verification Program (DSVP)



## ConsumerLab.com

### How to Read a ConsumerLab.com Approved Quality Product Seal:

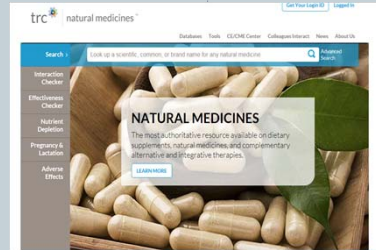


## IBIDS Database



- **International Bibliographic Information on Dietary Supplements**
  - Office of Dietary Supplements (ODS) at the NIH
  - Published, international, scientific literature
    - × Vitamins, minerals, and botanicals
  - Over 676,000 unique scientific citations abstracts
  - Three databases
    - × Full IBIDS database
    - × Peer-Reviewed Citations Only database
    - × IBIDS Consumer database

## Natural Medicines Research Collaboration <https://naturalmedicines.therapeuticresearch.com/>



<https://naturalmedicines.therapeuticresearch.com/>

## Case Study

- 16 yo female with chronic fatigue syndrome after a symptoms of a URI 18 months ago. She now has been diagnosed with fibromyalgia.
- She has been evaluated by
  - Her primary care physician
  - A Neurologist
  - Two rheumatologists
  - An otorhinolaryngologist
  - A nutritionist
  - A psychotherapist

- She has been treated with
  - Erythromycin twice
  - Cephalixin twice
  - Augmentin three times
  - Ciprofloxacin
  - Intravenous ceftriaxone
  - Oral nystatin
  - High doses of vitamins and a restriction diet

- Family wants to try turmeric, Coenzyme Q 10 and cannabinoid oil.
- Is this ok?



## Turmeric (Curcumin)

- **Uses:** osteoarthritis, rheumatoid arthritis (RA), dyspepsia, abdominal pain, Crohn's disease and ulcerative colitis, coronary artery bypass graft (CABG) surgery, hemorrhage, diarrhea, flatulence, abdominal bloating, loss of appetite, jaundice, hepatitis, ... radiation mucositis, radiation dermatitis, **fibromyalgia**, fatigue, leprosy, ...

## Turmeric (Curcumin)

- **Mechanism of Action:** antiinflammatory
- **Dose:** 500 mg four times daily
- **Adverse Effects:** constipation, dyspepsia, diarrhea, distension, gastroesophageal reflux, nausea, vomiting, pruritus, urticaria



Nieman DC et al.  
A commercialized dietary supplement alleviates joint pain in community adults: a double-blind, placebo-controlled community trial. *Nutr J.* 2013;12(1):154.

- **BACKGROUND:**
- The purpose of this study was to assess the effect of 8-weeks ingestion of a commercialized joint pain dietary supplement (Instaflex™ Joint Support, Direct Digital, Charlotte, NC) compared to placebo on joint pain, stiffness, and function in adults with self-reported joint pain. Instaflex™ is a joint pain supplement containing glucosamine sulfate, methylsulfonylmethane (MSM), white willow bark extract (15% salicin), ginger root concentrate, boswellia serrata extract (65% boswellic acid), turmeric root extract, cayenne, and hyaluronic acid.
- **METHODS:**
- Subjects included 100 men and women, ages 50-75 years, with a history (>3 months) of joint pain, and were randomized to Instaflex™ or placebo (3 colored gel capsules per day for 8 weeks, double-blind administration). Subjects agreed to avoid the use of non-steroidal anti-inflammatory drugs (NSAID) and all other medications and supplements targeted for joint pain. Primary outcome measures were obtained pre- and post-study and included joint pain severity, stiffness, and function (Western Ontario and McMaster Universities [WOMAC]), and secondary outcome measures included health-related quality of life (Short Form 36 or SF-36), systemic inflammation (serum C-reactive protein and plasma cytokines), and physical function (6-minute walk test). Joint pain symptom severity was assessed bi-weekly using a 12-point Likert visual scale (12-VS).
- **RESULTS:**
- Joint pain severity was significantly reduced in Instaflex™ compared to placebo (8-week WOMAC, 137% versus 116%, respectively, interaction effect  $P = 0.025$ ), with group differences using the 12-VS emerging by week 4 of the study (interaction effect,  $P = 0.0125$ ). Improvements in ability to perform daily activities and stiffness scores in Instaflex™ compared to placebo were most evident for the 74% of subjects reporting knee pain (8-week WOMAC function score, 139% versus 114%, respectively, interaction effect  $P = 0.027$ ; stiffness score, 130% versus 112%, respectively, interaction effect  $P = 0.081$ ). Patterns of change in SF-36, systemic inflammation biomarkers, and the 6-minute walk test did not differ significantly between groups during the 8-week study.
- **CONCLUSIONS:**
- Results from this randomized, double blind, placebo-controlled community trial support the use of the Instaflex™ dietary supplement in alleviating joint pain severity in middle-aged and older adults, with mitigation of difficulty performing daily activities most apparent in subjects with knee pain.

## Turmeric (Curcumin)

- Might reduce some symptoms of rheumatoid arthritis (RA), including pain, morning stiffness, walking time, and joint swelling compared to baseline.
- **Amalraj A. A novel highly bioavailable curcumin formulation improves symptoms and diagnostic indicators in rheumatoid arthritis patients: A randomized, double-blind, placebo-controlled, two-dose, three-arm, and parallel-group study. *J Med Food.* 2017;20(10):1022-1030.**
- Curcumin 500 mg twice daily reduces RA symptoms more than diclofenac sodium 50 mg twice daily after 8 weeks of treatment.
- **Chandran B. A randomized, pilot study to assess the efficacy and safety of curcumin in patients with active rheumatoid arthritis. *Phytother Res* 2012;26:1719-25.**

## CoEnzyme Q 10

- **Uses:** congestive heart failure (CHF), cardiotoxicity associated with doxorubicin chemotherapy, muscular dystrophy, increasing exercise tolerance, chronic fatigue syndrome (CFS), Lyme disease, autism, and chemotherapy-related fatigue.
- **Mechanism of Action:** Coenzyme Q10 is a fat-soluble compound with a chemical structure similar to vitamin K. Antioxidant.
- **Clinical Studies:**
- **Cordero MD. Can coenzyme Q10 improve clinical and molecular parameters in fibromyalgia? *Antioxid Redox Signal.* 2013;19(12):1356-61**
- Coenzyme Q10 300 mg daily for 40 days reduces pain by 52% to 56%, fatigue by 47%, morning tiredness by 56%, and tender points by 44% compared to baseline in patients with fibromyalgia

## Coenzyme Q 10

- **Lister RE. An open, pilot study to evaluate the potential benefits of coenzyme Q10 combined with Ginkgo biloba extract in fibromyalgia syndrome. *J Int Med Res* 2002;30:195-9.**
- Coenzyme Q10 200 mg in conjunction with ginkgo 200 mg orally daily for 12 weeks improves measures of quality of life such as physical fitness levels, emotional feelings, social activities, overall health, and pain



## Coenzyme Q 10

- **Dose:** 300 mg daily
- **Adverse Effects:** gastrointestinal side effects such as nausea, vomiting, diarrhea, appetite suppression, heartburn, and epigastric discomfort in less than 1% of patients.
- **Adverse effects can be minimized if total daily doses exceeding 100 mg are divided and administered two to three times per day**

## Cannabidiol

- Cannabidiol is a non-psychoactive constituent of Cannabis sativa, also known as marijuana.
- Over 80 constituents, known as cannabinoids, have been identified from the Cannabis sativa plant, of which delta-9-tetrahydrocannabinol (THC) is the major psychoactive compound.
- Cannabidiol makes up around 40% of cannabis extracts and has been investigated for a wide variety of therapeutic effects



## Cannabidiol

- **Uses:** anticonvulsant, antianxiety, antipsychotic, antinausea, and antirheumatoid arthritic
- **Clinical Studies:** D.C. Hammell. Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis. *Eur J Pain.* 2016 Jul; 20(6): 936–948.
- **Dose:** Cannabidiol 160 mg -300 mg daily
- **Adverse Effects:** dry mouth, hypotension, lightheadedness, orthostatic hypotension, psychomotor slowing, sedation, and somnolence.

## What would you recommend?

- Discussion...



## Case Study

- Heather is a 17 year old senior on the crew team. Her performance in crew has deteriorated recently and she is thinking about quitting. Her college applications are due and she is exhausted. She has been taking all sorts of herbs and supplements to get through the year both to stay awake and to get asleep as well as to keep her healthy.

## Caffeine



## Caffeine



- **Mechanism of Action:** Xanthine alkaloid which acts on external cell membrane and intracellularly through Calcium and cAMP pathways. Readily crosses blood brain barrier.
- **Uses:** Reduces drowsiness and restores alertness.
- **Clinical Studies:** Smith AP. 2005. Caffeine consumption may have benefits for performance and safety at work
- Burke LM. 2008 Caffeine and sports performance. *Appl Physiol Nutr Metab.*
- Astorino TA, Roberson DW. 2010. Efficacy of acute caffeine ingestion for short-term high-intensity exercise performance: a systematic review
- **Adverse Effects:** Anxiety, nervousness, withdrawal, insomnia, headaches, palpitations, GERD, peptic ulcers, irritability, tremulousness.

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Original article  
**Taking Stock of Dietary Supplements' Harmful Effects on Children, Adolescents, and Young Adults**

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 Keywords: Behavioral health; Dietary supplements; Adverse events

See Related Editorial on p.453

**ABSTRACT**

**Purpose:** The aim of the study was to evaluate the relationship between supplement categories and adverse events in children, adolescents, and young adults.  
**Methods:** This is a retrospective observational study using adverse event reports between January 2004 and April 2010 in the U.S. Food and Drug Administration Adverse Event Reporting System on food and dietary supplements database. We quantified the relative risks for severe medical events of dietary supplements sold for weight loss, appetite stimulation, energy enhancement, cognitive enhancement, emergency room visit, and/or required intervention to prevent permanent disability.  
**Results:** There were 977 single-supplement related adverse event reports affecting individuals aged between 0 and 20 years over 11 years (50.6% female; age range = 0–15 years, standard deviation = 12 years). Supplements sold for muscle building (28% sales [SE]), 2.7-fold confidence interval (CI) = 1.9–4.0), energy (28% = 2.6; 95% CI = 1.9–3.4), and weight loss (28% = 2.6; 95% interval CI) = 1.9–3.4 were associated with almost three times the risk for severe medical events compared with the placebo.  
**Conclusions:** Consumption of dietary supplements sold for weight loss, muscle building, and energy increased increased risks for severe medical events compared with placebo. Precaution enhancement or regulation is needed to reduce access and consumption among children, adolescents, and young adults.

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**Introduction**

Using Food and Drug Administration adverse event data, our study documents that dietary supplements sold for weight loss, muscle building, and energy use associated with almost three times the risk for severe medical events relative to placebo. Children, adolescents, and young adults should consult parents against using these supplements.

## Echinacea



- **Uses:** Approved in Germany as supportive therapy for upper respiratory infections, urogenital infections and wound healing
- **Mechanism of action:** May stimulate the alternate complement pathway and activate nonspecific T-cell. Echinacea may have immunomodulating effects and can inhibit viral replication, improve the motility of polymorphonuclear cells, enhance phagocytosis and natural killer cell activity.

## Echinacea

- **Clinical Studies:** Taylor JA. 2003. No difference in duration or estimation of severity between URIs treated with echinacea or placebo.
- Turner RB. 2005. Echinacea had no significant effect on either the occurrence of infection or the severity of illness.
- Cochrane Database Syst Rev. 2014 Feb Echinacea for preventing and treating the common cold. *Echinacea products have not here been shown to provide benefits for treating colds, although, it is possible there is a weak benefit from some Echinacea products: the results of individual prophylaxis trials consistently show positive (if non-significant) trends, although potential effects are of questionable clinical relevance.*



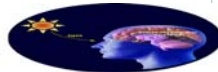
## Echinacea

- **Dose:** *Echinacea purpurea* leaf is 6 to 9 ml expressed juice tid. *Echinacea purpurea* root tincture; daily dose is 30 to 60 drops tid during a URI
- **Adverse effects:** Should not be used in those who are immunocompromised, in those with autoimmune diseases or in those allergic.

## Zinc

- **Uses:** Common Cold
- **Clinical Studies:** **Cochrane Review 2013**
- Randomised, double-blind, placebo-controlled trials using zinc for at least five consecutive days to treat, or for at least five months to prevent the common cold.
- Zinc administered within 24 hours of onset of symptoms reduces the duration of common cold symptoms in healthy people but some caution is needed due to the heterogeneity of the data.
- **Dose:** 75 mg per day
- **Adverse Effects:** bad taste and nausea, anosmia

## Melatonin



- **Uses:** jet lag, insomnia, shift-work disorder, circadian rhythm disorders in the blind, and benzodiazepine and nicotine withdrawal.
- **Mechanism of action:** In the brain, melatonin appears to increase the binding of gamma-aminobenzoic acid (GABA) to its receptors by affecting membrane characteristics, not by increasing the number of receptors
- **Clinical studies:** Petrie K 1989. Effect of melatonin on jet lag after long haul flights.
- Smits MG2001. Melatonin for chronic sleep onset insomnia in children: a randomized placebo-controlled trial.
- Ferracioli-Oda E1, Qawasmi A, Bloch MH. 2013. Meta-analysis: melatonin for the treatment of primary sleep disorders. PLoS One.
- **Dose:** 0.5- 5mg po HS
- **Adverse effects:** might inhibit ovulation, impair glucose utilization, decrease prothrombin activity, concomitant use of melatonin with alcohol, benzodiazepines, or other sedative drugs might cause additive sedation.

## Case Study

- Michael is a 11 year old with poor sleep, headaches, OCD and Tourette's Syndrome.
- The grandmother wants to try natural remedies for Michael because they seem to work for her. She has brought in butterbur, N- Acetyl cysteine (NAC), melatonin, Omega 3 capsules and St. Johns wort.
- Is this ok?



### Butterbur (*Petasites hybridus* root)

- **Uses:** Migraines
- **Mechanism of action:** anti-inflammatory effects by inhibiting leukotriene synthesis
- **Clinical Studies:** Pothmann R, Danesch U. Migraine Prevention in Children and Adolescents: Results of an Open Study With a Special Butterbur Root Extract. *Headache* 2005;45:196-203
- Oelkers-Ax R, Leins A, Parzer P, et al. Butterbur root extract and music therapy in the prevention of childhood migraine: an explorative study. *Eur J Pain* 2008;12:301-13

### N Acetylcysteine ( NAC)

- N-acetyl cysteine is used as an antidote for acetaminophen and carbon monoxide poisoning.
- It is used for bipolar disorder, schizophrenia, post-traumatic stress disorder (PTSD), substance use disorders, and **Tourette syndrome**.
- It is also used for reducing lipoprotein (a) levels in patients with hyperlipidemia, reducing risk of cardiovascular events in patients with end-stage renal disease (ESRD), bronchitis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, autism, adrenoleukodystrophy (ALD), hepatitis, kidney disease, ...
- for myoclonus epilepsy.... and detoxifying heavy metals such as mercury, lead, and cadmium

### N Acetylcysteine (NAC)

- Some clinical research shows that taking N-acetyl cysteine 900 mg daily for 4 weeks followed by 900 mg twice daily for 4 weeks and then 900 mg three times daily for 4 weeks improves symptoms of irritability in children with autism.
- Additional clinical research shows that taking N-acetyl cysteine 1200 mg daily plus risperidone for 8 weeks is more effective than risperidone alone for reducing irritability in children and adolescents with autism.
- Dose: 900-1200 mg BID
- Side Effects: gastrointestinal such as diarrhea, heartburn, nausea

### N Acetylcysteine (NAC)

- **Ghanizadeh A. Efficacy of N-Acetylcysteine Augmentation on Obsessive Compulsive Disorder: A Multicenter Randomized Double Blind Placebo Controlled Clinical Trial.** [Iran J Psychiatry](#). 2017 Apr; 12(2): 134–141.



### St. John's Wort

- **Uses:** Named after St. John the Baptist because it blooms around his feast day; used for depression.
- **Mechanism of action:** Inhibition of serotonin reuptake, MAO, 5 HT, dopamine, noradrenaline, GABA and glutamate.
- **Clinical Studies:** Cochrane Review 2005. Extracts of St. John's wort may be more effective than placebo; similar efficacy as standard antidepressants for mild to moderate depression. Major depression treatment effects may be minimal.

- **Dose:** 300mg (0.3% hypericin) tid
- **Adverse effects:** Induces cytochrome P450 3A and may increase metabolism of warfarin, cyclosporin, HIV protease inhibitors, theophylline, digoxin and oral contraceptives Can cause decreased platelet aggregation, serotonin syndrome, or photosensitivity.
- Rahimi R1, Abdollahi M. 2012. An update on the ability of St. John's wort to affect the metabolism of other drugs. *Expert Opin Drug Metab Toxicol*.



## Butterbur

- **Dose:** 50-75 mg daily in two or three divided doses for ages 8-9 years and 100-150 mg daily in two or three divided doses for ages 10-17 years
- **Adverse Effects:** gastrointestinal (belching, diarrhea, and stomach upset), dermal/allergic (itchy eyes, asthma, and pruritus)

## Magnesium

- **Uses:** Magnesium is a cofactor in more than 300 enzyme systems that regulate diverse biochemical reactions in the body, including protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation
- **Clinical Studies:** Sun-Edelstein C, Mauskop A. Role of magnesium in the pathogenesis and treatment of migraine. *Expert Rev Neurother* 2009;9:369-79
- Schürks M, Diener H-C, Goadsby P. Update on the prophylaxis of migraine. *Cur Treat Options Neurol* 2008;10:20-9.
- Holland S, Silberstein SD, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults. *Neurology* 2012;78:1346-53.
- **Dose:** 300 - 500 mg **citrate versus** daily po (soy beans, black beans, tofu, seeds, nuts, whole grains, shellfish )
- **Side effect:** Diarrhea, interactions with bisphosphonates, antibiotics and diuretics, \*PPI may reduce Mg Levels

## Omega 3 fatty acids-Docosahexanoic acid (DHA); Eicosapentanoic Acid (EHA)



- **Uses:** ADHD, depression, heart disease, prevention of macular degeneration
- **Mechanism of Action:** reduce serum triglycerides, promote normal neural and synaptic function
- **Clinical Studies:** Gabbay V. A double-blind, placebo-controlled trial of omega-3 fatty acids in Tourette's disorder. *Pediatrics*. 2012.
- **Dose:** Typical dose is 5 grams of oil containing 169-563 mg of EPA and 72-312 mg of DHA twice daily.  
**Adverse Effects:** Fishy taste, belching, nosebleeds, nausea, and loose stools. High doses of fish oils might also decrease blood coagulation

Fraguas D, Diaz-Caneja CM, Pina-Camacho L, et al. Dietary Interventions for Autism Spectrum Disorder: A Meta-analysis. *Pediatrics*. 2019;144(5):e20183218

## Dietary Interventions for Autism Spectrum Disorder: A Meta-analysis

David Fraguas, MD, PhD,<sup>1,2</sup> Constanza M. Díaz-Caneja, MD, PhD,<sup>1,2</sup> Laura Pina-Camacho, MD, PhD,<sup>1,2</sup> Carmen Morero, MD, PhD,<sup>1,2</sup> Manuel García-Rodríguez, MD, PhD,<sup>1,2</sup> María Jesús, MD, PhD,<sup>1,2</sup> Francisco González-Vergara, PhD,<sup>1,2</sup> María del Mar Martín, MD, PhD,<sup>1,2</sup> Robert E. Hendrick, MD,<sup>1,2</sup> Gilio Arraigo, MD, PhD,<sup>1,2</sup> María Fernández, MD, PhD<sup>1,2</sup>

**OBJECTIVE:** Dietary interventions such as restrictive diets or supplements are common treatments for young people with autism spectrum disorder (ASD). Evidence for the efficacy of these interventions is still controversial.

**DESIGN:** To assess the efficacy of specific dietary interventions on symptoms, functions, and clinical domains in subjects with ASD by using a meta-analytic approach.

**SETTING:** Ovid Medline, PsycINFO, Embase databases.

**MEASUREMENTS AND MAIN RESULTS:** We selected placebo-controlled, double-blind, randomized clinical trials assessing the efficacy of dietary interventions in ASD published from database inception through September 2017.

**CONCLUSIONS:** Outcome variables were subsumed under 4 clinical domains and 17 symptoms and/or functions groups. Hedge's adjusted g values were used as estimates of the effect size of each dietary intervention relative to placebo.

**RESULTS:** In this meta-analysis, we examined 27 double-blind, randomized clinical trials, including 1028 patients with ASD: 543 in the intervention arms and 485 in the placebo arms. Participant-weighted average age was 7.1 years. Participant-weighted average intervention duration was 10.6 weeks. Dietary supplementation (including omega-3, vitamin supplementation, and/or other supplementation), omega-3 supplementation, and vitamin supplementation were more efficacious than the placebo at improving several symptoms, functions, and clinical domains. Effect sizes were small (mean Hedge's g for significant analyses was 0.31), with low statistical heterogeneity and low risk of publication bias.

**CONCLUSIONS:** Methodologic heterogeneity among the studies in terms of the intervention, clinical measures and outcomes, and sample characteristics.

**CONCLUSIONS:** This meta-analysis does not support nonspecific dietary interventions as treatment of ASD but suggests a potential role for some specific dietary interventions in the management of some symptoms, functions, and clinical domains in patients with ASD.

## Omega -3

- Derbyshire E. **Brain Health across the Lifespan: A Systematic Review on the Role of Omega-3 Fatty Acid Supplements.** [Nutrients](#). 2018 Aug; 10(8): 1094.
- The present systematic review collated evidence from 25 randomized controlled trials (n = 3633) published since 2013. Compared with control groups, omega-3 supplementation generally correlated with improvements .

## What would you recommend?

- Discussion...



## WEBSITES

- [www.consumerlab.com](http://www.consumerlab.com)
- [www.naturalmedicines.therapeuticresearch.com](http://www.naturalmedicines.therapeuticresearch.com)
- [www.nccih.nih.gov](http://www.nccih.nih.gov)
  - [Ibooks- Herbs at a glance](#)
- [www.herbmed.org](http://www.herbmed.org)
- [www.herbs.org](http://www.herbs.org)

## AAP Section Complementary, Holistic and Integrative Medicine (SOIM)

- **Mission:** to support the mission of the AAP "to attain optimal physical, mental, and social health and well being for all infants, children, adolescents, and young adults" by:
  - promote policies to enhance patient-centered care;
  - integrate evidence-based, safe and effective complementary therapies into high quality pediatric practice;
  - educate clinicians and families; advocating for appropriated payment for safe and effective services; and
  - respectfully collaborate with diverse health professionals dedicated to enhancing the health of infants, children, and adolescents.



## Questions?

- [cora.breuner@seattlechildrens.org](mailto:cora.breuner@seattlechildrens.org)  
206 999 1208



## Case Study

- 7 yo male was diagnosed with leukemia last month and his family wants to use herbal remedies to support him through his chemotherapy.
- What suggestions can you offer?

## Peppermint

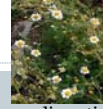
- **Uses:** Irritable bowel syndrome, colic, nausea, decongestant, cough suppressant, anxiolytic, topical analgesic for headache and myalgia.
- **Mechanism of action:** Calcium channel blocker in GI smooth muscle, vapors stimulate sensory nerve endings in nasal mucosa, triggers cold receptors on the skin causing a sensation of coolness and analgesia
- **Clinical Studies:** Kline 2001. In a study comparing enteric peppermint capsules with placebo in children with IBS, 75% experienced improvement in their symptoms.
- Khanna R, MacDonald JK, Levesque BG. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. Clin Gastroenterol 2014 ;48(6):505-12
- **Dose:** One to 2 enteric-coated capsules containing 0.2 ml of peppermint oil taken 2 to 3 times a day
- **Adverse effects:** Infantile apnea when applied under/in nose, heartburn, mild rectal burning.

## Arnica



- **Uses:** inflammation and immune system stimulation associated with bruises, aches, and sprains.
- **Mechanism of Action:** Sesquiterpene lactones, which are esters of helenalin and 11,13-dihydrohelenalin. These constituents seem to have anti-inflammatory, analgesic, and platelet-inhibitory effects
- **Clinical Studies:** Adkison JD. The effect of topical arnica on muscle pain. *Ann Pharm* 2010;44:1579-84.  
**Dose:** 2 grams flowerheads in 100 mL water; as a poultice, the tincture of arnica is diluted three to ten times with water
- **Adverse Effects:** irritation of mucous membranes, drowsiness, stomach pain, vomiting, diarrhea, allergic reaction in individuals sensitive to the Asteraceae/Compositae family.

## Chamomile



- **Uses:** Cultivated worldwide as a sedative, anti-spasmodic, anti-inflammatory and wound healing agent
- **Mechanism of Action:** Chamazulene: antispasmodic; Apigenin-anxiolytic; Bisabolol- anti-inflammatory
- **Clinical Studies:** Savino F. A randomized double-blind placebo-controlled trial of a standardized extract of *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis* (ColiMil) in the treatment of breastfed colicky infants. *Phytother Res* 2005;19:335-40.
- Amsterdam JD. [A randomized, double-blind, placebo-controlled trial of oral \*Matricaria recutita\* \(chamomile\) extract therapy for generalized anxiety disorder](#) *Journal of Clinical Psychopharmacology*. 2009 Aug;29(4): 378-382.

## Chamomile

- **Dose:** Infusion can be prepared from fresh or dried flower heads, usually 2–3 teaspoons in a cup of boiling water, infused for 10 minutes and taken orally three times a day.
- **Adverse Effects:** People sensitive to ragweed, chrysanthemums or other members of the Compositae family are more prone to develop contact allergies to chamomile

## Zingiber officinale (Ginger)



- **Uses:** Antiemetic, antinausea, circulatory stimulant, anti-inflammatory
- **Mechanism of Action:** Ginger contains antiemetic, anti-inflammatory, and analgesic properties. Promotes the flow of bile into the intestine through contraction of the gallbladder. Pharmacologically active components of the oleoresin include gingerols.
- **Clinical Studies:** Borrelli F, 2005 Four of the 6 RCTs showed superiority of ginger over placebo in pregnancy induced nausea and vomiting.
- **Dose:** 2 to 4 grams of fresh root daily (0.25 to 1.0 g of powdered root) or 1.5 to 3.0 mL (30 to 90 drops) tincture daily.
- **Adverse Effects:** May cause heartburn, decreased platelet aggregation. Topical application may cause contact dermatitis in sensitive patients.



## What would you recommend?

- Discussion...

