

## Natural Medicines Food-Drug Interactions and Other Interesting Stuff

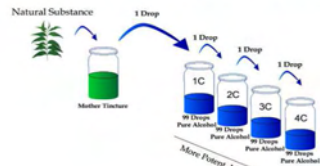
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## Homeopathy

- Like treats Like
- More dilute = More potent
- Potentization – serial dilutions...

### How Remedies are Made - Potentizing



Each vial is shaken vigorously after each dilution is made.

## Why is it important for Dietitians to know about Natural Medicines?

## Because they are popular...

**32% of kids (birth to 18 years old):  
79% of college students<sup>2</sup>**

**69% of US adults<sup>3</sup>  
44% of men >20 years old<sup>4</sup>  
53% of women >20 years old<sup>4</sup>  
70%-83% of older adults<sup>4,5</sup>**

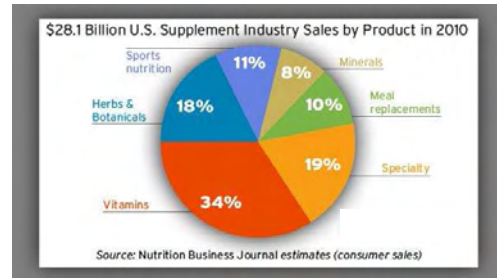
**55% of older adults use ≥3 supplements<sup>5</sup>**

1. Picciano MF, et al. Arch Pediatr Adolesc Med. 2007;161:978-985.  
2. Johnson SK, et al. J Am Coll Health. 2006;55:163-8.  
3. Council for Responsible Nutrition. Annual CRN Consumer Survey. Mar 13, 2012 <http://www.crnusa.org>  
4. Bailey RL, et al. J Nutr. 2011;141:261-6.  
5. Nahin RL, et al. J Am Geriatr Soc. 2009;57:1197-1205.

Because they are popular...

Condition	Adults	Children
Arthritis	83%	72%
Asthma	25%	
Breast cancer	69-97%	
CV disease	46%	
Diabetes	41%	
Lung disease	55%	
Menopause	80%	
Seizure disorder	56%	62%
Sickle cell disease		47%
Stroke survivors	46%	
Surgery patients	40%	

Because they are popular...



Nutrition Business Journal Data for 2010. Nutrition Business Journal. Sep 1, 2011.

DS Use... Impact on Health Choices

People who use dietary supplements have a greater sense of *invulnerability* and may tend to make poorer healthy behavior choices.

Chiou WB, et al. Psychol Sci. 2011;22(8):1081-6.

Impact on Drug Therapy

52%-85% of older people use Rx meds and dietary supplements concomitantly...

69% of those who use Rx drugs and dietary supplements do not discuss these combinations with a medical professional.

Qato DM, et al. JAMA. 2008;300:2867-78.  
Nahin RL, et al. J Am Geriatr Soc. 2009;57:1197-1205.

## Dieticians and Dietary Supplements

300 registered dietitians surveyed in 2009...

- 97% “ever recommended” dietary supplements
  - bone health (70%)
  - fill “nutrient gaps” (67%)
  - overall health and wellness (49%)
  - lowering cholesterol (46%)
  - heart health (46%)
  - digestive/GI health (39%)
  - diabetes or glucose control (27%)
  - eating disorders (19%)

Dickinson A, et al. Nutrition Journal 2012, 11:14.  
<http://www.nutritionj.com/content/pdf/1475-2891-11-14.pdf>

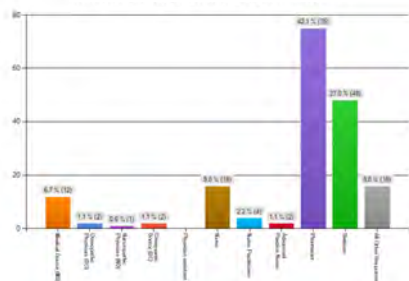
## Dieticians and Dietary Supplements

300 registered dietitians surveyed in 2009...

- 95% expressed interest in learning more about dietary supplements
  - ✓ interactions with drugs
  - ✓ regulation
  - ✓ drug-induced nutrient depletion

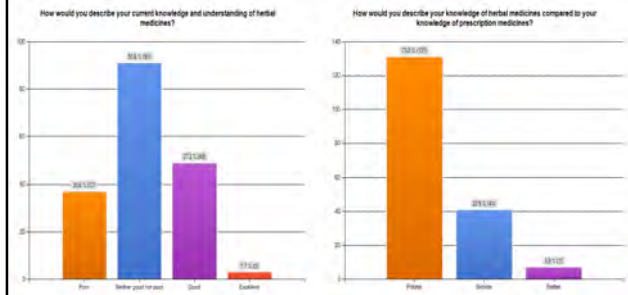
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## Hawai'i Health Professionals

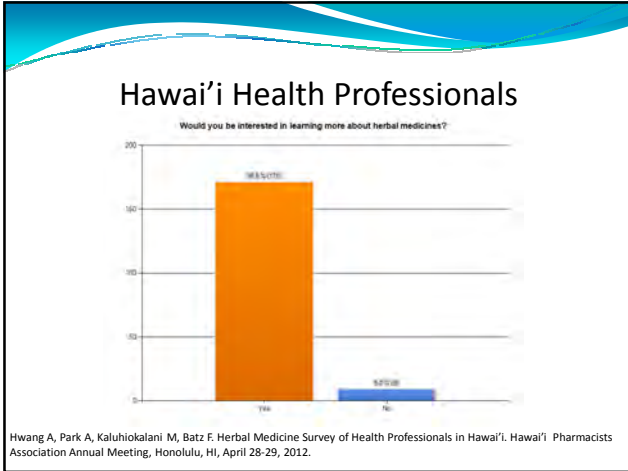


Hwang A, Park A, Kaluhiokalani M, Batz F. Herbal Medicine Survey of Health Professionals in Hawai'i. Hawai'i Pharmacists Association Annual Meeting, Honolulu, HI, April 28-29, 2012.

## Hawai'i Health Professionals



Hwang A, Park A, Kaluhiokalani M, Batz F. Herbal Medicine Survey of Health Professionals in Hawai'i. Hawai'i Pharmacists Association Annual Meeting, Honolulu, HI, April 28-29, 2012.



### Public Perceptions

- >60%... supplements have been tested
- 65%... supplements are proven safe
- 63%... supplements are proven effective
- 54%... supplements are FDA-approved

National telephone survey of 1,500 respondents; University of Connecticut Center for Survey Research & Analysis; presented at the Obesity Society's Annual Meeting, Boston, MA, October 2006.

### Public Perceptions

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- 65%... supplements are proven safe
- 63%... supplements are proven effective
- 54%... supplements are FDA-approved

**FALSE**

National telephone survey of 1,500 respondents; University of Connecticut Center for Survey Research & Analysis; presented at the Obesity Society's Annual Meeting, Boston, MA, October 2006.

### DSHEA

1994- Dietary Supplement Health and Education Act (DSHEA)

... amendment to the Food, Drug and Cosmetic Act

... created a new regulatory framework for the safety and labeling of dietary supplements.

### DSHEA

Products intended to supplement the diet.

May contain one or more dietary ingredients: vitamins, minerals, herbs or other botanicals, amino acids, or other substances, or their constituents.

Intended to be *taken by mouth* as a pill, capsule, tablet, or liquid...  
excludes: sublingual, rectal, sprays, creams, ointments, patches, etc.

Front panel of label must state "dietary supplement".

### DSHEA

Manufacturers...

- ✓ responsible to ensure product safety and claims not false or misleading
- ✓ not required to register with the FDA

FDA ... responsible for taking action against unsafe dietary supplement products after they reach the market

Established no minimum standards for dietary supplement manufacturing.

### DSHEA

March 2003  
 FDA proposed Labeling and Manufacturing Standards requiring manufacturers to:

- ✓ Evaluate the identity, purity, quality, strength, and composition of ingredients and finished products.
- ✓ Products containing contaminants, or not containing the ingredient(s) stated on the label, are considered adulterated.

June 2007 → Aug 2010  
 Final rule for dietary supplement cGMPs published with phase-in period.

### DSHEA

Claims not required... Drug claims not allowed.

Allowed claims:

- ❖ Approved health claims
- ❖ Structure/function claims... *disclaimer must appear on label:*

"These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

## Proposed Legislation

Feb 2010 - Dietary Supplement Safety Act (McCain)... failed

May 2010 - Dietary Supplement Full Implementation and Enforcement Act of 2010 (Harkin/Hatch)... failed

Future ???

## Adverse Events Reporting

1994 DSHEA- FDA responsible for post-marketing surveillance; no program in place requiring manufacturers to monitor for, or report, adverse events.

Dec 2007- Dietary Supplement and Non-Prescription Drug Consumer Protection Act

- Requires manufacturers to report *SERIOUS* adverse events (death, birth defects, life-threatening illness) involving DS and OTCs to FDA... exempts retailers from mandatory reporting.

## Adverse Events Reporting



Safety Information & Adverse Event Reporting  
[www.fda.gov/medwatch](http://www.fda.gov/medwatch)  
 1.800.FDA.1088

## DS Product Quality

	as of 2001	2007 +
Calcium	(29/33) 88%	(8/8) 100%
Chondroitin	(0/2) 0%	(3/9) 33%
Creatine	(11/ 13) 85%	(8/12) 67%
Fish Oils	N/A	(17/24) 71%
Ginkgo leaf S/E	(7/30) 23%	(3/7) 43%
Ginseng	(9/21) 43%	(11/17) 65%
Glucosamine	(10/10) 100%	(10/10) 100%
Glucos/Chondr combo	(7/13) 54%	(7/11) 64%
Multivitamins	N/A	(21/31) 68%
Probiotics	N/A	(17/25) 68%
SAME	(7/13) 54%	(7/10) 70%
St. John's wort	N/A	(7/13) 54%
Saw palmetto	(17/27) 63%	(10/13) 77%
Vitamin C	(22/26) 85%	(22/23) 96%

## Contamination

- Heavy Metals...
  - arsenic, cadmium, lead, mercury
- Environmental Exposure...
  - pesticides, manufacturing waste, etc
- Toxic plant materials...

## Adulteration

- NSAIDs
- glucocorticoids
- benzodiazepines
- oral hypoglycemic agents
- warfarin
- bumetanide
- anabolic steroids
- sibutramine
- PDE-5 inhibitors

## Voluntary Quality Programs



USP



Contents Tested

NSF



Be Sure It's CL Approved

ConsumerLab.com

## Supplement-Drug Interactions

#1 Herb: St. John's Wort

Induces cytochrome P450 3A4 (CYP 3A4) + others

↓ serum levels of...

amitriptyline, cyclosporine, digoxin, indinavir, theophylline, warfarin, and others.

Reduces effectiveness of oral contraceptives!

### Supplement-Drug Interactions

**#1 Drug: Warfarin (Coumadin)**

↑ warfarin effects  
chondroitin, danshen, devil's claw, dong quai, garlic, ginkgo, glucosamine, grapefruit, papain, pomegranate, vitamin E

↓ warfarin effects:  
coenzyme Q10, green tea (large amounts), noni, Panax ginseng, St. John's wort

### Supplement-Drug Interactions

Unwanted/undesirable effects → Negative Interactions

Desired/desirable effects → Positive Interactions

### Supplement-Drug Interactions

**Undesirable Interactions**

Grapefruit juice → multiple drugs  
[www.powernetdesign.com/grapefruit](http://www.powernetdesign.com/grapefruit)

Ginkgo biloba → blood thinners, trazodone

Garlic (medicinal amounts) → blood thinners, hypoglycemic agents

### Supplement-Drug Interactions

**Desirable Interactions**

Niacin + 'statins' (additive effects... Advicor)

Probiotics to prevent/reduce antibiotic-associated diarrhea



## Drug Influences on Nutrient Levels and Depletion

Marketing Tool  
or  
Clinically Relevant Concept

Example: Statins - Coenzyme Q10 levels

## Food-Drug Interactions Middle Age → Elders

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- ACE inhibitors (ACEIs)  
Angiotensin II receptor blockers (ARBs)
- ✓ Salt substitutes- ↑ risk of hyperkalemia
  - ✓ Potassium rich foods... noni juice - ↑ risk of hyperkalemia

## Food-Drug Interactions Middle Age → Elders

- HMG CoA reductase inhibitors (statins)
- ✓ Grapefruit juice- ↑ risk of all side effects
  - ✓ Red yeast rice- ↑ risk of all side effects

### Food-Drug Interactions Middle Age → Elders

metformin (Glucophage, etc)

- ✓ Excessive EtOH- ↑ risk of metabolic acidosis
- ✓ Guar gum- ↓ absorption... separate by >6 hours

### Food-Drug Interactions Middle Age → Elders

hydrocodone/acetaminophen (Vicodin, etc)

- ✓ EtOH + hydrocodone- ↑ risk of CNS depression
- ✓ EtOH + acetaminophen- ↑ risk of liver damage

### Food-Drug Interactions Middle Age → Elders

antidepressants with serotonergic activity

- ✓ 5-HTP supplements- ↑ risk of serotonergic side effects
- ✓ Tryptophan supplements- ↑ risk of serotonergic side effects

### Food-Drug Interactions Middle Age → Elders

warfarin (Coumadin, etc)

- ✓ Melatonin supplements- ↑ risk of bleeding
- ✓ Garlic- ↑ risk of bleeding
- ✓ Ginkgo supplements- ↑ risk of bleeding
- ✓ Grapefruit juice- ↑ risk of bleeding
  
- ✓ Co-enzyme Q10 supplements- ↓ effectiveness
- ✓ Green tea (large amounts)- ↓ effectiveness
- ✓ Noni- ↓ effectiveness

## Food-Drug Interactions Middle Age → Elders

benzodiazepines and other sedative/hypnotics

- ✓ Melatonin supplements- ↑ risk of CNS depression
- ✓ Tryptophan supplements-
  - ↑ risk of CNS depression
  - (BDZs) ↑ risk of sexual disinhibition, reversible dyskinesias, reversible Parkinsonian-like rigidity

## Food-Drug Interactions Middle Age → Elders

diuretics

Licorice-

- ↑ sodium and water retention... ↑ BP
- ↑ potassium excretion and risk of hypokalemia

## Drugs with Anticholinergic Activity in Elders

↑ risk of...

- ❖ confusion
- ❖ hallucinations
- ❖ sedation
- ❖ blurred vision
- ❖ dry mouth
- ❖ urinary retention
- ❖ constipation

Drugs with medium-to-high anticholinergic activity ... →

Class	Drugs	Class	Drugs	Class	Drugs
<b>Antiarrhythmics</b>	Disopyramide	<b>Antimuscarinics (Overactive Bladder Agents)</b>	Darifenacin Flavoxate Oxybutynin Tolterodine	<b>Antiseizure Drugs</b>	Carbamazepine Oxcarbazepine
<b>Antidepressants</b>	Amiriptryline Clomipramine Desipramine Doxepin Imipramine Nortriptyline Paroxetine Protriptyline Trimipramine	<b>Antiparkinson Agents</b>	Amantadine Benztropine Trihexyphenidyl	<b>Gastrointestinal agents</b>	Atropine Belladonna Cimetidine Dicyclomine Hyoscyamine Loperamide Prochlorperazine Promethazine Propantheline Ranitidine
<b>Antihistamines</b>	Brompheniramine Carbincoxamine Chlorpheniramine Clemastine Cyproheptadine Dimenhydrinate Diphenhydramine Hydroxyzine Meclizine Pyrilamine Triprolidine	<b>Antipsychotics</b>	Clomipramine Chlorpromazine Clozapine Fluphenazine Loxapine Olanzapine Perphenazine Pimozide Quetiapine Thiothixene Trifluoperazine	<b>Muscle relaxants</b>	Baclofen Carisoprodol Cyclobenzaprine Methocarbamol Orphenadrine Tizanidine
Drugs with Potential Anticholinergic Activity. Pharm Lett.2011;27(12):271206.				<b>Opioids</b>	Meperidine

