Complementary and Alternative Medicine in Gastroenterology

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Definition and Terminology

“A group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine”
- National Center for Complementary and Alternative Medicine (www.nccam.nih.gov)

I. Whole Medical Systems
(acupuncture, homeopathic medicine, naturopathic)

II. Mind-Body Medicine
(yoga, meditation, hypnosis, cognitive behavioral therapy, stress management)

III. Biologically Based Treatments
(probiotics, prebiotics, herbal remedies, dietary supplements)

IV. Manipulative and Body-Based Practices
(osteopathy, massage, biofeedback)

V. Energy Medicine
(prayer, Reiki, Qigong, magnet therapy, light therapy, colorpuncture)
CAM statistics

**Total Health Care Spending**
- $2.2 Trillion
  - **Reimbursed**
  - Conventional Out-of-Pocket*: $268.6 billion
  - CAM Out-of-Pocket: $33.9 billion

† Reimbursed spending includes employer and individual private insurance, Medicare, Medicaid, State Children's Health Insurance Program, other private and public spending, and some CAM.

CAM statistics

**CAM Out-of-Pocket Spending: Self-Care* vs. Practitioner Costs**
- **Non-vitamin, Nonmineral, Natural Products**: $14.8 billion (43.7%)
- **Yoga, Tai Chi, Qi Gong Classes**: $4.1 billion (12.0%)
- **Homeopathic Medicine**: $2.9 billion (8.6%)
- **Relaxation Techniques†**: $0.2 billion (0.6%)
- **Practitioner Costs**: $11.9 billion (35.1%)

Total Costs = $33.9 billion
- Total Self-Care Costs: $22.0 billion (64.9%)
- Total Practitioner Costs: $11.9 billion (35.1%)

* Self-Care costs include CAM products, classes, and materials.
† Relaxation techniques include meditation, guided imagery, progressive relaxation, and deep breathing exercises.
CAM statistics

Out-of-Pocket Costs for Select CAM Therapies*

- Nonvitamin, Nonmineral, Natural Products (Practitioner and Self-Care) $15.4 billion
- Massage (Practitioner) $4.2 billion
- Yoga, Tai Chi, QI Gong Classes (Self-Care) $4.1 billion
- Chiropractic or Osteopathic Manipulation (Practitioner) $3.9 billion
- Homeopathic Medicine (Practitioner and Self-Care) $3.1 billion

* Totals for nonvitamin, nonmineral, natural products and homeopathy include both CAM practitioner costs and costs of purchasing CAM products. Totals for massage and chiropractic and osteopathic manipulation are only CAM practitioner costs. Totals for yoga, tai chi, and qigong classes are only the cost of purchasing CAM products.

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CAM statistics

Out-of-Pocket Spending

- Other Conventional Care* $177.8 billion
- Prescription Drugs* (Rx Drugs) $47.6 billion
- Nonvitamin, Nonmineral, Natural Products (NMNHMP) $34.9 billion
- CAM Practitioner Visits $17.2 billion
- Other CAM+ $7.2 billion

- Conventional Medicine
- CAM


+ Other CAM includes yoga, tai chi, qigong classes, homeopathic medicine, and cranial techniques.
Growth in the Supplement Industry

Cumulative % increase

**How did we get here?**

**Dietary Supplement Health Education Act -1994 - Federal law**

- Dietary supplements do not have to prove safety or efficacy so long as they do not make any claims to treat a disease
- The manufacturer of a dietary supplement or dietary ingredient is responsible for ensuring that the product is safe before it is marketed.
- FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market.

<table>
<thead>
<tr>
<th>CAM use in Gastroenterology Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GI Patients and CAM Therapy</strong></td>
</tr>
<tr>
<td>Pts use CAM in addition to traditional medications although no insurance reimbursement</td>
</tr>
<tr>
<td>Pts are <em>not</em> primarily interested in scientific evaluation of treatments</td>
</tr>
<tr>
<td>Pts often do not inform their GI MDs of CAM usage</td>
</tr>
<tr>
<td>Most research on CAM and GI illness is on IBS + functional diseases; research on CAM + IBD is increasing</td>
</tr>
<tr>
<td>Herbal therapy = most common CAM treatment for all GI disorders</td>
</tr>
<tr>
<td><strong>Primary Reasons for CAM Use</strong></td>
</tr>
<tr>
<td>Ineffectiveness of conventional treatment</td>
</tr>
<tr>
<td>Direct disease-related benefits</td>
</tr>
<tr>
<td>Interest in holistic (multidisciplinary) treatment</td>
</tr>
<tr>
<td>Belief that CAM is safer</td>
</tr>
<tr>
<td>Greater control over one’s health</td>
</tr>
<tr>
<td>Side effects of conventional medications</td>
</tr>
<tr>
<td>End or avoid steroid medication (IBD pts)</td>
</tr>
</tbody>
</table>

[Hilsden et al., Inflamm Bowel Dis, 2011; Kearney and Brown-Chang, Nat Clin Pract Gastro and Hep 2008]

[Hilsden et al., Inflamm Bowel Dis, 2011; Tilisch K, Gut 2005]
Sources of Beliefs of the Public

- For most people “naturalness” is a guarantee of harmlessness
- Widespread availability in health food stores and supermarkets
- High level of acceptability of risks, under-reporting of risks
- Infrequency of litigation against CAM practitioners
- Lack of critical thinking – Benefit vs. Risk
  - Education
  - Lack of medical practitioner interest or feedback to patients
  - Lack of open communication
  - Belief that CAM is irrelevant to medical therapy

Classification of the risks associated with CAM

- Commission risks
  - Removal of appropriate therapy (e.g. loss of benefit, morbidity, death)
  - Incorrect prescribing (e.g. failure to observe contraindications)
  - Negligent practice (e.g. use of infected and contaminated products)
- Omission risks
  - Misdiagnosis
  - Failure to refer
  - Failure to explain risks or precautions
CAM and Irritable Bowel Syndrome

Mind Body Techniques: Gut-Directed Hypnotherapy

- There are 5 good quality and 22 additional studies re: therapeutic effects of IBS hypnotherapy
- Results = significant improvement in IBS in at least half of pts
- Psych symptoms + QoL + overall function improved post treatment
- Therapeutic gains = maintained for most pts over many yrs
- Mechanism of action of IBS hypnotherapy = poorly defined

Webb, Cochrane Reviews, 2007
Moser, AJG, 2013

Hypnotherapy and IBS

- RCT of 51 vs 49 pts with gut directed hypnotherapy vs supportive treatment
- Treatment group – slightly younger, better social functioning, less duration of IBS

<table>
<thead>
<tr>
<th>% improved</th>
<th>Hypnosis</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>At end of 12 sessions</td>
<td>60.8%</td>
<td>40.9%</td>
</tr>
<tr>
<td>At 15 mos of f/u</td>
<td>54.3%</td>
<td>25.0%</td>
</tr>
</tbody>
</table>

Moser, AJG, 2013
Mindfullness Based Stress Reduction and IBS

- RCT of 36 vs 39 women pts with MBSR vs support group
- Also significant improvements in QoL, psychological distress and visceral anxiety at 3 months follow up

![Graph showing overall IBS severity over time with a comparison between support and mindfulness groups.](image)

Gaylord SA, AJG 2011: 106;1678

CAM and Irritable Bowel Syndrome

Acupuncture

- Effectiveness in IBS may be due to alteration in visceral sensation and motility through stimulation of somatic nervous system and vagus nerve
- Conclusions from two recent randomized studies of acupuncture among IBS patients: [Lembo et al., 2009; Schneider et al. 2006]

* Compared to no treatment, acupuncture OR sham acupuncture is superior at relieving IBS symptoms
* No significant differences between acupuncture and sham acupuncture
* Ritual of acupuncture (i.e. nonspecific placebo effects) may be effective in relieving IBS symptoms
How about placebo effects in IBS?

- RCT of 37 vs 43 IBS pts with 2 pills of open-placebo vs no pills for 21 days
- Additional statistically significant differences in adequate relief, symptom severity and quality of life

Kaptchuk, PlosOne, 2010

How about placebo effects in IBS?

- 104 patients genotyped for catechol-O-methyltransferase (which affects dopamine availability in prefrontal cortex) from a RCT of 262 IBS pts in 3 groups: No treatment, Placebo (limited Rx), Placebo+ Supportive Provider (augmented Rx)

Hall, PlosOne, 2012
How diverse are we?

- Unique fingerprints - Stable over short periods of time
- Species and strain differences rather than taxa differences in healthy individuals

Diet Drives Gut Bacteria

- Animal protein, saturated fat
- Plant-based nutrition; high carbohydrate, low meat/dairy

Both long-term and short-term diet may be important
Alcoholism and Colonic Mucosal Microbiome

What is a probiotic?

- Probiotics are "live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host."

World Health Organization and the Food and Agriculture Organization of the United Nations
Use of Probiotics in GI Disease

- Premature infant diseases (e.g., NEC)
- Lactose maldigestion
- Antibiotic-associated diarrhea
  - *C. difficile* colitis
- Traveler’s diarrhea
- Irritable bowel syndrome
- Inflammatory bowel diseases
- Colon cancer

Probiotics in IBS

- >20 RCT present with a variety of lactobacilli, bifidobacteria, streptococci alone or in combination
- Meta-analyses results vary:
  - Moayyedi et. al. - 19 studies
    - RR not improving = 0.71 (95% CI 0.57 to 0.88); NNT = 4 (95% CI 3.0 to 12.5)
  - Clarke et. al.
    - 34/42 RCTs efficacious on IBS in one endpoint
  - Brenner et. al. – 16 RCT
    - 2 studies of *Bifidobacterium infantis* showed significant improvements

Moayyedi, Gut 2010
Clarke APET 2012
Brenner, AJG 2009
### Crohn’s disease - Active disease

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>Study groups</th>
<th>Remission rate (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plein (1993)</td>
<td>17</td>
<td>R</td>
<td>S. boulardii (750 mg)</td>
<td>9 NR NR</td>
<td>Reduction in DAI</td>
</tr>
<tr>
<td>Malchow (1997)</td>
<td>28</td>
<td>R, OL</td>
<td>Placebo</td>
<td>12 75 92 NS</td>
<td>Concomitant steroids used; no differences in relapse</td>
</tr>
<tr>
<td>Gupta et al. (2000)</td>
<td>4</td>
<td>OL</td>
<td>LGG (&gt;10^10 CFU)</td>
<td>24 100 - -</td>
<td>Pediatric trial</td>
</tr>
<tr>
<td>Fujimori (2007)</td>
<td>10</td>
<td>OL</td>
<td>Symbiotic (Bifidobacteria + Lactobacilli + psyllium)</td>
<td>- 52 - -</td>
<td>70% response rate, Reduction in CDAI</td>
</tr>
<tr>
<td>Steed (2010)</td>
<td>35</td>
<td>R, DB</td>
<td>Symbiotic (B. longum+Senergy 1)</td>
<td>24 62 45</td>
<td>NR, calculate d p=0.68(c hi-sqr) Reduction in mean CDAI, histology scores, and tissue TNF alpha expression</td>
</tr>
</tbody>
</table>

### Crohn’s disease - Post-op recurrence

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>Study groups</th>
<th>Relapse rate (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prantera et al. (2002)</td>
<td>45</td>
<td>R, DB</td>
<td>LGG (4-92 g)</td>
<td>12 17 11 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Marteau et al. (2006)</td>
<td>98</td>
<td>R, DB</td>
<td>L. johnsonii (&gt;10^9 CFU)</td>
<td>6 49 64 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Van Gossum et al. (2007)</td>
<td>70</td>
<td>R, DB</td>
<td>L. johnsonii (&gt;10^6 CFU)</td>
<td>3 15 14 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Chermesh et al. (2007)</td>
<td>30</td>
<td>R, DB</td>
<td>Synbiotic 2000*</td>
<td>24 25 20 NS</td>
<td>NS</td>
</tr>
</tbody>
</table>
**Crohn’s disease - Maintenance of remission**

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>S. boulardii (1 g) + Mesalazine (3 g)</th>
<th>Mesalazine (3 g)</th>
<th>6</th>
<th>6</th>
<th>38</th>
<th>0.04</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guslandi et al. (2000)</td>
<td>32</td>
<td>R, OL</td>
<td>S. boulardii Placebo</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Garcia Viela (2008)</td>
<td>34</td>
<td>R, OL</td>
<td>VSL#3 (6 g)</td>
<td>12</td>
<td>20</td>
<td>40</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Schultz et al. (2004)</td>
<td>11</td>
<td>R, DB</td>
<td>LGG (2X10⁸ CFU) Placebo</td>
<td>6</td>
<td>60</td>
<td>67</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Bousvaros et al. (2005)</td>
<td>75</td>
<td>R, DB</td>
<td>LGG (&gt;10⁹ CFU) Placebo</td>
<td>24</td>
<td>31</td>
<td>17</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Malchow (1997)*</td>
<td>28</td>
<td>R, OL</td>
<td>E. coli Nissle</td>
<td>12</td>
<td>33</td>
<td>63</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Fujimori (2006)</td>
<td>10</td>
<td>OL</td>
<td>Symbiotic with Bifidobacter and Lactobacillus</td>
<td>-</td>
<td>13</td>
<td>30</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Ulcerative colitis - Active disease**

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>S. boulardii (750 mg)</th>
<th>68%</th>
<th>-</th>
<th>-</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Kato (2004)</td>
<td>20</td>
<td>R, DB</td>
<td>Fermented milk (100 ml) Placebo</td>
<td>12</td>
<td>40</td>
<td>30</td>
<td>NS</td>
</tr>
<tr>
<td>Furia (2005)</td>
<td>18</td>
<td>R, DB</td>
<td>Synergy 1 (8 g) + Syngian (2X10⁷ CFU) Placebo</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Fujimori (2009)</td>
<td>120</td>
<td>R, OL</td>
<td>Bifidum (2X10⁶ CFU) or probiotic powder (4 g) Bifidum (2X10⁶ CFU) or probiotic powder (4 g)</td>
<td>4</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Rembachen (1999)*</td>
<td>116</td>
<td>R, DB</td>
<td>E. coli Nissle (1X10⁹ CFU)</td>
<td>4</td>
<td>32</td>
<td>25</td>
<td>NS</td>
</tr>
<tr>
<td>Mathela (2006)</td>
<td>90</td>
<td>R, DB</td>
<td>VSL#3 enema - 40 vs 30 vs 20 ml</td>
<td>4</td>
<td>33 vs 44 vs 27</td>
<td>16</td>
<td>0.04</td>
</tr>
<tr>
<td>Vilea (2009)*</td>
<td>29</td>
<td>R, DB</td>
<td>VSL#3 (weight based) Placebo</td>
<td>12</td>
<td>21</td>
<td>73</td>
<td>0.01</td>
</tr>
</tbody>
</table>
| Sood (2006)*       | 14F | R, DB, IC, CA VSL#3 (3.6 X10¹⁰ CFU) Placebo | 12 | 43 | 16 | 0.001 |Multicenter study. 30% of patients in placebo group showed improvement in UCDAI, increased mucosal healing seen treatment (62% vs 15%)

* Also in maintenance trials
UC and VSL#3 in active disease

N=144
12 weeks
RCT
Adjunctive treatment

Ulcerative Colitis - Maintenance of remission

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>Study groups</th>
<th>Duration (months)</th>
<th>Relapse rate %</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kruis (1997)</td>
<td>120</td>
<td>R, DB, DD</td>
<td>E. coli/Nissle (200 mg)</td>
<td>Mesalazine (1.5g)</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Rombaut (1999)</td>
<td>196</td>
<td>R, DB, DD</td>
<td>E. coli/Nissle (&gt;10^10 CFU)</td>
<td>Mesalazine (2.6g)</td>
<td>12</td>
<td>32</td>
</tr>
<tr>
<td>Kruis et al. (2004)</td>
<td>327</td>
<td>R, DB, DD</td>
<td>E. coli/Nissle (200 mg)</td>
<td>Mesalazine (1.5g)</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td>Ishikawa (2003)</td>
<td>21</td>
<td>R</td>
<td>Fermented milk (100 ml)</td>
<td>Placebo</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>Cui et al. (2004)</td>
<td>30</td>
<td>R, DB</td>
<td>BIFICO mixture (1.26g)</td>
<td>Placebo</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Zocco et al. (2006)</td>
<td>180</td>
<td>R, OL</td>
<td>LGG (&gt;10^10 CFU) or LGG + mesalazine</td>
<td>Mesalazine (2.4 g)</td>
<td>12</td>
<td>15 or 17</td>
</tr>
<tr>
<td>Meihe (2009)</td>
<td>29</td>
<td>R, DB</td>
<td>VSL#3 (weight based)</td>
<td>Placebo</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>Venturi (1999)</td>
<td>20</td>
<td>OL</td>
<td>VSL#3 (6 g)</td>
<td>-</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Shanahan (2006)</td>
<td>157</td>
<td>R, DB</td>
<td>L. salivaria (&gt;10^10 CFU) + B. infantis (&gt;10^6 CFU)</td>
<td>Placebo</td>
<td>12</td>
<td>~50</td>
</tr>
</tbody>
</table>
## Clinical Trials in Pouchitis

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Trial design</th>
<th>Indication</th>
<th>Intervention</th>
<th>Control</th>
<th>Duration (months)</th>
<th>Relapse/Disease rate (%)</th>
<th>Notes/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gionchetti et al. (2000)</td>
<td>40</td>
<td>R, DB</td>
<td>Maintenance</td>
<td>VSL#3 (6 g)</td>
<td>Placebo</td>
<td>9</td>
<td>15 100 &lt;0.001</td>
<td>Longer remission recurrence after 3 m of stopping</td>
</tr>
<tr>
<td>Mimura et al. (2004)</td>
<td>36</td>
<td>R, DB</td>
<td>Maintenance</td>
<td>VSL#3 (6 g)</td>
<td>Placebo</td>
<td>12 15 94 &lt;0.01</td>
<td>Concomitant cipro/flagyl in both arms; longer remission; better QOL</td>
<td></td>
</tr>
<tr>
<td>Gionchetti et al. (2003)</td>
<td>40</td>
<td>R, DB</td>
<td>Prophylaxis</td>
<td>VSL#3 (3g)</td>
<td>Placebo</td>
<td>12 10 40 &lt;0.05</td>
<td>4x reduced risk; better QOL</td>
<td></td>
</tr>
<tr>
<td>Kuisma et al. (2003)</td>
<td>20</td>
<td>R, DB</td>
<td>Maintenance</td>
<td>LGG (&gt;10^10 CFU)</td>
<td>Placebo</td>
<td>3 NR NR NR</td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td>Friedman &amp; George (2000)</td>
<td>10</td>
<td>OL</td>
<td>Active</td>
<td>LGG + FOS (1 tab each)</td>
<td>-</td>
<td>1 - - -</td>
<td>100% remission</td>
<td></td>
</tr>
<tr>
<td>Gasenlik et al. (2004)</td>
<td>117</td>
<td>CL</td>
<td>Prophylaxis</td>
<td>LGG (300 mg)</td>
<td>Historical</td>
<td>36 7 29 0.01</td>
<td>4x reduced risk</td>
<td></td>
</tr>
<tr>
<td>Leake et al. (2005)</td>
<td>52</td>
<td>OL</td>
<td>Active</td>
<td>Fermented milk (500 ml)</td>
<td>-</td>
<td>1 NR - -</td>
<td>Less symptoms</td>
<td></td>
</tr>
<tr>
<td>Shen et al. (2005)</td>
<td>31</td>
<td>OL</td>
<td>Maintenance</td>
<td>VSL#3 (6 g)</td>
<td>-</td>
<td>8 81 - -</td>
<td>19% stable</td>
<td></td>
</tr>
<tr>
<td>Gionchetti (2007)</td>
<td>23</td>
<td>CL</td>
<td>Active</td>
<td>VSL#3 (6 g)</td>
<td>-</td>
<td>1 - - -</td>
<td>69% remission</td>
<td></td>
</tr>
<tr>
<td>Pronio (2008)</td>
<td>31</td>
<td>R, OL</td>
<td>Maintenance</td>
<td>VSL#3 (6 g)</td>
<td>-</td>
<td>12 NR -</td>
<td>Better PSN; increased regulatory T cells in mucosa</td>
<td></td>
</tr>
</tbody>
</table>

### Plagues in the clinical data in IBD and probiotics

- Most not controlled or blinded or multicenter
- Reports very vague
- Limited no of subjects, short follow-ups
- Some contaminated by concomitant drugs such as steroids
- Most not independently confirmed by others who are not inventors/sponsors
Peppermint Oil (PO)

- Active ingredient of peppermint oil = methol which has calcium channel blocking activity and relaxes smooth muscle

- From *Mentha X piperita* L flowers; available OTC as Colpermin® and Elanco LOK®

- Better tolerated than conventional smooth muscle relaxants, since no anticholinergic side effects

- Systematic review of 4 trials found significant + consistent improvement in IBS symptoms with relative risk of only 0.43, compared to placebo (95% confidence interval, 0.32-0.59).  
  Ford et al, *Gastro & Hep*, 2010

Iberogast for functional dyspepsia

- Mixture of 9 herbs
- 8 weeks
- N=315
- 5 patients - 7AEs (abdominal pain, pruritus, sore throat, alopecia, hypersensitivity, hypertension, gastrointestinal pain)

VonArnim, AJG 2007
Otilinger, WMW 2013
Turmeric- Curcumin for adenoma prevention

- Phase IIa, open label trial
- 20 patients studied with aberrant crypt foci in rectum before and after treatment in 2 phases

Other Herbal Studies

- Compound herbal formulas in IBS
  - Chinese herbal medicine – RDBPC- 16 weeks – IBS-all
  - Padma Lax- RDBPC-3 months- IBS-C
- Milk Thistle for alcoholic, hepatitis B and C
  - Liver-related mortality was significantly reduced by milk thistle in all trials (RR 0.50, 95% CI 0.29 to 0.88), but not in high-quality trials (RR 0.57, 95% CI 0.28 to 1.19)
- Turmeric
  - 2 g dose decreases relapse at 6 mos in UC patients on 5-ASAs
  - In a 60 pt RCT, decreases ALT in patients with elevated LFTs
- Boswellia
  - Efficacy non-inferior to 5-ASAs in Crohn’s disease, reduction in CDAI
  - Similar ~75% improvement with Boswellia vs. sulfasalazine in UC

Bensoussan, JAMA, 1998
Salon, Digestion, 2002
Rambaldi, Cochrane DR, 2007
Hame, Clin Gastro Hepat, 2006
Jim, BMC-CAM, 2013
Gerhardt, Z Gastroenterol, 2001
Safety of Individual Therapies

Little information available!
Most probably minor reactions per estimates

Direct Effects of Commonly Used Herbs

- **Gingko**
  - GI symptoms (nausea, vomiting)
  - Bleeding
  - Headache, Seizures
- **St. John’s wort**
  - Nausea
  - Allergic reactions, Photosensitivity
- **Ginseng**
  - Nausea, Diarrhea
  - Headache, BP changes
  - Mastalgia/Vaginal Bleeding
- **Green tea**
  - Emesis, diarrhea
- **Shark cartilage**
  - Emesis
  - Constipation
  - Hepatitis
- **Echinacea**
  - Anaphylaxis
- **Saw palmetto**
  - Constipation
  - Nausea
  - Rare diarrhea
  - Hypertension, Urinary retention
- **Kava**
  - Yellow discoloration
  - Abdominal pain
  - Hepatitis/Fulminant hepatic failure
  - Dizziness, stupor, Extrapyramidal effects
- **Laetrile**
  - Emesis
  - Headache, Dizziness, Obtundation, Dermatitis
### GI side effects

<table>
<thead>
<tr>
<th>Herb</th>
<th>Main use</th>
<th>GI side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloe</td>
<td>Constipation, IBS</td>
<td>Diarrhea/Abdominal cramps</td>
</tr>
<tr>
<td>Anise</td>
<td>Dyspepsia, ulcers, cough</td>
<td>N/V</td>
</tr>
<tr>
<td>Black cohosh</td>
<td>Menopause, joint aches</td>
<td>N/V/Diarrhea</td>
</tr>
<tr>
<td>Chitosan</td>
<td>Weight loss</td>
<td>Bloating/Constipation</td>
</tr>
<tr>
<td>Fewerfew</td>
<td>Migraine, menstrual, fever, worms</td>
<td>Mouth ulcers</td>
</tr>
<tr>
<td>Garlic</td>
<td>HTN</td>
<td>N/ Heartburn/Flatulence</td>
</tr>
<tr>
<td>Gentian</td>
<td>Digestive aid, appetite stimulant</td>
<td>N/V</td>
</tr>
<tr>
<td>Hydrangea</td>
<td>Diuretic, Mood disorders, Euphoria</td>
<td>N/V</td>
</tr>
<tr>
<td>Mistletoe</td>
<td>Low BP</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Mormon tea</td>
<td>Diarrhea, Tonic</td>
<td>Constipation</td>
</tr>
<tr>
<td>Pancreatic enzymes</td>
<td>Digestive aid</td>
<td>Colonic strictures, ulcers</td>
</tr>
<tr>
<td>Papain</td>
<td>Digestive aid</td>
<td>Ulcers</td>
</tr>
<tr>
<td>Penny royal</td>
<td>Abortifacient</td>
<td>N/V/Diarrhea</td>
</tr>
<tr>
<td>Poke root</td>
<td>Cancer, Constipation</td>
<td>V/Abdominal pain</td>
</tr>
<tr>
<td>Senega</td>
<td>Cough</td>
<td>N/V/Diarrhea</td>
</tr>
<tr>
<td>Shavegrass</td>
<td>Diuretic</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Yellow dock</td>
<td>Constipation</td>
<td>N/Diarrhea</td>
</tr>
</tbody>
</table>

### Hepatotoxicity

<table>
<thead>
<tr>
<th>Herb</th>
<th>Main use</th>
<th>GI side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapparal</td>
<td>Joint aches</td>
<td>Cholestasis, hepatitis</td>
</tr>
<tr>
<td>Chinese skullcap</td>
<td>Stress</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Comfrey</td>
<td>Arthritis</td>
<td>Venocclusive disease</td>
</tr>
<tr>
<td>Germander</td>
<td>Obesity</td>
<td>Fulminant hepatitis</td>
</tr>
<tr>
<td>Greater celandine</td>
<td>Diuretic</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Kava</td>
<td>Anxiety</td>
<td>Fulminant hepatic failure</td>
</tr>
<tr>
<td>Mistletoe</td>
<td>Low BP, Tension</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Paeonia</td>
<td>Psoriasis</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Pennyroyal</td>
<td>Abortifacient</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Sassafras</td>
<td>Tonic</td>
<td>HCC</td>
</tr>
<tr>
<td>Senecio herbal tea</td>
<td>Tonic</td>
<td>Veno-occlusive disease</td>
</tr>
<tr>
<td>Valerian</td>
<td>Mood disorders, Stress, Sleep</td>
<td>Hepatitis</td>
</tr>
</tbody>
</table>
**Major Herb-Drug Interactions**

- St. John’s Wort - 10/17
  - Lowers concentrations of cyclosporin, amitriptyline, digoxin, indinavir, warfarin, theophylline
  - Intermenstrual bleeding with OCP
  - Serotonin syndrome with loperamide or SSRIs
- Garlic
  - Lowers concentration of warfarin, saquinavir
  - Changes pharmacokinetics of acetaminophen
  - Causes hypoglycemia with chlorpropamide
- Ginkgo
  - Causes bleeding with warfarin, HTN with a thiazide diuretic
  - Reduced iron absorption
- Ginseng
  - Interacts with MAO-I, hypoglycemic agents, warfarin
- Kava
  - Potentiates sedative effects

**Other GI related Herb/Supplement-Drug Interactions**

- Fewerfew
  - potentiates warfarin
- Tamarind
  - potentiates ASA related GI bleed
- Ginger, Devil’s claw
  - reduced iron absorption
- Echinacea
  - Anabolic steroid, MTX, Amiodarone, Ketoconazole related hepatotoxicity
- Capsaicin/chili
  - Ace inhibitor related cough
- Yohimbe
  - Interacts with meperidine as a MAO-I inhibitor
- Licorice
  - Steroid related water retention and hypokalemia
What has happened so far?

- FDA recalled more than 100 dietary supplements for reasons:
  - Eosinophilia myalgia syndrome
  - Digitalis intoxications
  - Hypervitaminosis D
  - Salmonella infection
- PC-SPES for advanced prostate cancer – pulled out in 2002-contaminated with warfarin and diethylstilbestrol
- Ephedra
  - CVS effects and CNS toxicity
- Kava
  - Hepatitis/ Fulminant liver failure
- Chinese herb nephropathy

Other dangerous treatments

- Androstenedione – steroid effects
- LipoKinetix- Liver failure
- Tiratricol/TRIAC/Triax metabolic accelerator – Hyperthyroidism
- Ancom antihypertensive – Contains Reserpine, HCTZ
- Viga/Vinarol- Contains Sildenafil
- Cholestin- Contains Lovastatin
- Sleeping Buddha – Contains Estazolam
- Indian Healing Clay- Neonatal tetanus reported
- Nettle/Koo Sar – Lead contamination
Acupuncture

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Reported cases or Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at site of insertion</td>
<td>0.9-45%</td>
</tr>
<tr>
<td>Persistent pain after insertion</td>
<td>2.3%</td>
</tr>
<tr>
<td>Tiredness</td>
<td>2.3-41%</td>
</tr>
<tr>
<td>Petechiae/Ecchymosis/Hematoma</td>
<td>0.03-38% -- 15%</td>
</tr>
<tr>
<td>Fainting</td>
<td>0.9-7%</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.01-0.2%</td>
</tr>
<tr>
<td>Failure to remove needle</td>
<td>0.09%</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 cases-0.001%</td>
</tr>
<tr>
<td>Surgical needle removal</td>
<td>2 cases- 0.001%</td>
</tr>
<tr>
<td>Burns due to moxibustion</td>
<td>1 case</td>
</tr>
<tr>
<td>Infection</td>
<td>?</td>
</tr>
</tbody>
</table>

Legal Issues
CAM Usage and Role of GI Physician

When Interacting with Patients:

- Inquire about what CAM intervention/s pt is/was using
- Determine why pt has opted for CAM intervention/s and if pt has been noncompliant with medication
- Maintain open-minded, non-critical stance toward pt’s CAM use
- Discuss potential side effects of CAM use (i.e. herbal products)
- Stay current on evidence-based CAM research: www.nccam.nih.gov

Definition of CAM under law

- No legislature or court defined CAM per se
- CAM professions are regulated mostly by state legislature
- Existing malpractice rules have been applied to CAM
- Potential liabilities
  - Aiding and abetting unlawful practice of medicine
    - Scope of practice under state law
      - Familiarize yourself with state laws/licensure
      - Watch for problems
    - Nonstandard therapy = Substandard care/Negligent care
      - Last resort
      - Benefit vs risk profile
How to protect oneself?

- Determine clinical risk level
- Document literature supporting the therapeutic choice
- Obtain informed consent
  - Charell vs. Gonzales
- Obtain written agreement to concomitant CAM use
- Continue to offer to monitor the patient
  - Charell vs. Gonzales
- Inquire about CAM provider’s competence

Resources on safety

- PubMED
- Herbal PDR
- Herbal Medicine: Expanded Commission E Monographs
- Adverse effects of herbal drugs – 3 volumes-Heidelberg, Germany- 1997- De Smet
- FDA MedWatch Program - [www.fda.gov/medwatch](http://www.fda.gov/medwatch)
Other resources on herbal products

www.herbmed.org
www.consumerlab.com
The national council against health fraud
www.ncahf.org
www.quackwatch.org