Tending the Garden Within: Cultivating GI Wellness

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“Let food be thy medicine”

Hippocrates, b. 460 BC

“All disease begins in the gut”

Cardiovascular disease
Liver disease

Numerous factors are influencing the complex gut ecosystem:
• Lifestyle
• Food
• Immune priming
• Host metabolic signaling

Gut microbiota

Neuroendocrine system

Depression
Anxiety
Alzheimer disease
Parkinson disease
Neurodegenerative diseases
Multiple sclerosis
Diabetes
Immune resistance
Obesity
Low-grade inflammation
Arthritis
Allergy
Eczea

Nature Reviews: Gastroenterology & Hepatology

New York Times, Phil Marden, 12/29/2016 "Gut Makeover for a New Year"
Food-like substances

Tolerance, Craving, Withdrawal

![Image of 7UP bottle]

![Image of various snacks]

Meat commonly consumed vegetables among U.S. consumers, 2014

- Fresh
- Canned
- Frozen
- Dried
- Potato Chips

Pounds per person:

- Potatoes
- Tomatoes
- Onions
- Head lettuce
- Sweet corn
- Carrots
- Romaine and leaf

Saffron (Crocus sativus) for depression: a systematic review of clinical studies and examination of underlying antidepressant mechanisms of action

The Role of Curcumin Administration in Patients with Major Depressive Disorder: Mini Meta-Analysis of Clinical Trials
In vitro and animal studies
- Inhibit pro-inflammatory mediators, signaling pathways, cell surface adhesion molecules
- Inhibit intestinal epithelial cell disruption
- Accelerate gastric emptying
- Increase ghrelin level
- Inhibit H. pylori infection
- Inhibit intestinal contraction
- Decrease visceral pain

TURMERIC

Human studies
- Improve dyspepsia and gastric inflammation
- Increase hydrogen-producing colonic microbiota
- Retain remission in Ulcerative Colitis


The Gut-Brain-Microbiota Axis

Stress
Poor gut function
Inflammation
Gut bacteria “Dysbiosis”
• Stomach “hollow muscular sac that initiates the second phase of digestion”
• Chemically breaks down food

Actually....
• Sophisticated endocrine organ
• Gastric and esophageal microbiome
• Role in appetite, food absorption, metabolism and obesity
• Barrier against pathogen entrance into GI tract

“peptic esophagitis ... resulting from the irritant action on the mucosa of free hydrochloric acid and pepsin.”

New Hypothesis: inflammation precedes injury

- Rats—not chemical injury at surface, but submucosal lymphocytes that progresses to surface
- Human esophageal cells briefly exposed to acid and bile—not damaged but secrete cytokines.
- 12 patients with erosive disease taken off PPIs:
  - All developed T lymphocyte–predominant esophageal inflammation and basal cell and papillary hyperplasia without loss of surface cells.
- ?—Not chemical damage.
- Cytokines attract immune cells → inflammation

Chili

- Chili used 10-300 times more in Asia
- TRPV-1 receptors (Transient Receptor Potential Vanilloid-1)
- TRPV-1 receptors increased in
  - visceral hypersensitivity syndromes like functional heartburn and IBS
  - inflammed gut mucosa like esophagitis
- Capsaicin desensitizes Substance P from TRPV-1 receptors
- Receptors become refractory in general
Chili desensitizes:

- **GERD** and **Functional Dyspepsia**: symptoms worse initially
- After 3 weeks: epigastric pain, fullness and nausea improved
- **IBS**: Acute ingestion increased symptoms
- After 6 weeks reduced abdominal pain and bloating

Intact gut barrier

Small Intestine Bacterial Overgrowth “SIBO”
### SIBO: herbs and spices = Rifaximin

<table>
<thead>
<tr>
<th>Regimen 1</th>
<th>Regimen 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Thyme</td>
<td>• French Tarragon</td>
</tr>
<tr>
<td>• Oregano</td>
<td>• Indian Tinospora</td>
</tr>
<tr>
<td>• Sage</td>
<td>• Indian Tinospora</td>
</tr>
<tr>
<td>• Lemon Balm</td>
<td>• French Tarragon</td>
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<tr>
<td>• Orange Gage</td>
<td>• Thyme</td>
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<tr>
<td>• Copia</td>
<td>• Pau D’Arco</td>
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<tr>
<td>• Berberine</td>
<td>• Stringing Nettle Extract</td>
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<tr>
<td>• Ginger</td>
<td>• Olive (leaf)</td>
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<tr>
<td>• Licorice</td>
<td>• Dill</td>
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<tr>
<td>• Chinese Rhubarb</td>
<td>• Senega</td>
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<tr>
<td>• Scullcap</td>
<td>• Wormwood, Java Bruere, Chinese Pulsatilla, Picrorhiza exotica, Cutchtree, Melastoma, Yarrow</td>
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**Intact gut barrier**

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### Increased Intestinal Permeability

- Obesity
- Inflammatory Bowel Disease
- Celiac disease
- Irritable Bowel Syndrome
- Non-Alcoholic Fatty Liver Disease, NASH
- Small Intestine Bacterial Overgrowth (SIBO)
- Alcoholism
- Parkinson’s
- Type 1 diabetes
- HIV
- Autism
- Several Cancers
- Many others

turmeric
Proposed sites of action of curcumin in attenuating disruption of intestinal epithelial barrier function.


Small Intestine Micronutrient Absorption

*Black pepper (piperine), red pepper (capsaicin), ginger*

- Increased:
  - brush border membrane fluidity
  - activity of membrane enzymes
  - microvilli length/perimeter
  - absorptive capacity of small intestine

Healthy gut bacteria
Take some bacteria-free mice and transplant gut bacteria

14 days later..
Take bacteria-free mice and colonize with the microbiota of obese vs. nonobese mice...

Spices/Microbiota

- Spice-specific phytochemicals
- Most polyphenols
- Vast majority cannot be absorbed by small intestine
- 95% pass into colon where they are fermented by gut bacteria
- Beneficial effects attributable to dietary (poly)phenols depend on their biotransformation by the gut microbiota

Spices & Microbiota: prebiotic aspects

- Dietary factors influence the relative abundance of bacterial groups
- Prebiotic = "substances that induce the growth or activity of microorganisms that contribute to the well being of the host"
- Enhance beneficial lactobacilli and bifidobacteria—either by being substrate or affect bacterial metabolism/enhancing nutrient intake
- Reduce gram negatives and pathogens
  - Black pepper, cayenne pepper, cinnamon, ginger, Mediterranean oregano, rosemary and turmeric tested in vitro for prebiotic/antimicrobial activity.
  - All except turmeric promoted the growth of Bifidobacterium spp. and Lactobacillus spp.
  - Oregano, black pepper, cayenne and ginger both promoted lacto. And bifido. species and suppressed pathogenic species.
