Herbal Considerations to Effectively Treat SIBO and SIFO

Instructor:
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Disclaimer

- CMO at SIBOtest.com
- I hold no financial interest in any of the information presented today

Pros and cons of herbal medicines

**Pros:**
- Herbs often have multiple effects, e.g. antibacterial and antifungal, anti-inflammatory and antioxidant, etc.
- Mostly cause less damage to the microbiome
- Have evolved with bacteria and thus have overcome many of their resistance strategies
- Can be combined to address multiple issues

**Cons:**
- Can be more costly due to length of treatment
- Patients self-medicating with inferior herbal products can be cause for concern due to contamination (heavy metals, etc.)
- Allergies, salicylates, oxalates
- Doses often vary depending on formulation (standardized extract vs whole plant)
- Limited research in SIBO and SIFO, more research in IBS in general

Botanical Mechanisms of overcoming Bacterial Resistance

- **Bacterial efflux pumps actively remove antibiotics and other substances out of the cell:**
  - Examples of herbs which inhibit or down regulate these: Berberine containing plants, Thyme, Juniper, Licorice, Green Tea
- **Alterations in bacterial cell wall permeability – gram neg bacteria down regulate porin expression which limits antibiotic entry into the cell.**
  - Examples of herbs which alter bacterial cell wall: Bearberry, Goldenseal, Usnea
- **Plasmids: strains of bacterial DNA that contain resistance information. Highly mobile and passed on to other bacteria**
  - Examples of herbs that modulate bacterial DNA: Barberry, Golden Seal, Oregon Grape, Thyme

Antibiotics for SIBO- out of the frying pan and into the fire?

Long term damage to the microbiome with repeated antibiotic courses

“The fecal microbiome was severely affected by most antibiotics: for months, health-associated butyrate-producing species became strongly underrepresented. Additionally, there was an enrichment of genes associated with antibiotic resistance. Clearly, even a single antibiotic treatment in healthy individuals contributes to the risk of resistance development and leads to long-lasting detrimental shifts in the gut microbiome.”

The Culprits

Predominant SIBO bacteria isolated on duodenal aspirate (Pimentel, 2015):

- **gram positive:**
  - Enterococcus spp
  - other studies also identified Streptococcus and Staphylococcus

- **gram negative:**
  - Proteus mirabilis
  - E.coli
  - Klebsiella pneumoniae

- Methanobrevibacter smithii (methane)

Co-morbid SIFO

candida spp and other fungal spp


Herbal uses in SIBO and SIFO

- **Antimicrobials**
  - *Antibacterial/antifungals/antimethanogen*

- **Anti-inflammatory, antioxidants, immune modulators:**
  - curcumin, green tea
  - *Herbal Prokinetics*

- **Anti-spasmodics/carinatives:** chamomile, caraway seeds

Anti-microbials

1. Berberine containing herbs
2. Garlic
3. Oregano
4. Clove
5. Pomegranate
6. Artemisia annua
7. Usnea
8. Horopito
Berberine containing herbs

Clinically well established for reducing hydrogen
Phellodendron amurense, Mahonia aquafolium (Oregon grape), Coptis chinensis (Goldthread), Berberis vulgaris (Barberry), Hydrastis canadensis (Golden Seal)

• Berberine: different berberine alkaloids have different actions
  • effective against: E.coli, Klebsiella p., P. aeruginosa, Staphylococcus spp, Streptococcus spp and candida spp
  • interferes with the adhesion of LTA (lipoteidoic acid), a ligand responsible for the adherence of Streptococci to epithelial cells

Berberine - MOA

1. Efflux pump inhibition
2. Bacterial cell membrane permeability modification
3. Inhibition of biofilm formation
4. Inhibition of bacterial replication
5. Anti-virulence properties via quorum quenching

Buhner, S (2012) Herbal Antibiotics, USA; Storey Publishing
Goldenseal (Hydrastis canadensis L.) extracts synergistically enhance the antibacterial activity of berberine via efflux pump inhibition.

Berberine containing herbs

• poorly absorbed from GI thus ideal for local infections
• Mucous membrane “tonifying” effect
• Berberine is also
  • Antiinflammatory
  • Antioxidant

Ingredient in many “gut antimicrobial formulas” – ensure a daily dose of 2-3 grams of berberine if included with other strong antimicrobials. Most herbal formulas only deliver around 500mg

Tincture: standard dose is 30-50ml a week, may have to go much higher than that

Caution:

High berberine can have hypoglycemic effects and also inhibit MOA enzyme

Berberine and hydrogen reduction on LBT

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<th>Sample #</th>
<th>ppm H2</th>
<th>ppm CH4</th>
<th>Combined</th>
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Sample | ppm H2 | ppm CH4 | Combined |
--------|--------|---------|----------|
Control  | 1      | 0       | 3        |
20 min   | 2      | 9       | 10       |
40 min   | 3      | 1       | 7        |
60 min   | 4      | 1       | 7        |
80 min   | 5      | 1       | 7        |
100 min  | 6      | 1       | 7        |
120 min  | 7      | 8       | 13       |
140 min  | 8      | 10      | 19       |
T100 min | 9      | 16      | 25       |
T120 min | 10     | 19      | 29       |
Allium sativum (Garlic)

- Allium sativum is antifungal, antibacterial, antiviral
- Allicin (diallyl thiosulphinate) – widely studied constituent of Garlic
  - Highly volatile compound (unstable) -
- Main MOA - inhibition of thiol containing enzymes which maintain intracellular redox state within bacterial cells.
- Disrupts electrochemical potential of yeast cells - causes apoptosis
- Do not use “aged garlic” or fresh garlic extracts - not as effective and contain Fructans (high FODMAP)
  - Allisure 360mg BID- TID
  - clinically proven to lower methane

Syzygium aromaticum (Clove)

- contain 15-20% of clove is essential oil, primarily Eugenol.
- Anti-proliferative, antiinflammatory
- Active against a wide variety of gram (+) and (-) bacteria, including K.pneumoniae, E.coli, Proteus mirabilis, Streptoccocus, Staphyloccocus, Bacillus cereus, and H.pylori
- Broad spectrum anti-fungal - candida spp, Aspergillus, Dermatophytes (trichophyton etc)
- Anti-histamine: inhibits mast cell degranulation and reduction of mesenteric Mast cell infiltration

Garlic extract and methane reduction

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Syzygium aromaticum (Clove)

- Gastroprotective: 
  - stimulates gastric mucous production
  - Antibacterial against H.pylori
- Motility
  - Helpful in IBS-C
  - Increase gastrointestinal muscle propulsion similar to metoclopramide and carbachol – cholinergic activity
- Dose
  - 10-15ml per week of a 1:2 extract
  - Caution: excess doses can increase bleeding time, some evidence of CYP3A4 inhibition


Punica granatum (Pomegranate)

- Juice, rind and seed used
- Active constituents: ellagic acid glycosides and ellagitannins, other tannins, flavonoids
- Gram-positive bacteria: Staphylococcus aureus, Streptococcus spp, and Bacillus spp
- Gram-negative bacteria: E.coli, Campylobacter jejuni, Salmonella spp, Shigella spp, Vibrio spp, Klebsiella pneumonia, Pseudomonas aeruginosa, Yersinia enterocolitica, H.pylori
- Fungal: candida spp
- Parasitic infections: Giardia spp, Blastocystis spp, Entamoeba h., Cryptosporidium parvum, and more.

- "Significantly enhances growth of Lactobacillus spp, Bifidobacterium breve and Bifidobacterium infantis while inhibiting the growth of pathogenic clostridia and Staphylococcus aureus"
- Therapeutic Dose: 40-80ml/week (10ml daily) of a 1:2 tincture


Artemisia annua (Qing Hao)

- Active constituents: essential oils and sesquiterpenoids (artemisinins)
- Classically used for parasites, malaria
- Antimicrobial activity against
  - Gram-positive bacteria: Staphylococcus aureus, Streptococcus spp, and Bacillus spp
  - Gram-negative bacteria: E.coli, Salmonella spp, Klebsiella pneumonia, Pseudomonas aeruginosa, Proteus spp
- Antiparasitic against: Toxoplasma gondii, Schistosoma (blood fluke), Fasciola hepatica (liver fluke), Plasmodium f.
- Immunomodulation- inhibits NO, INO and NF-kB
- Therapeutic Dose: 20-50ml/week 1:2 extract


Usnea spp (Old Man’s Beard)

- Over 600 Usnea spp – found on every continent
- Primary active constituent: usnic acid
- Primarily active against gram positive bacteria: Bacillus spp, Clostridium spp, Enterococcus spp, Listeria monocytogenes, Staphylococcus spp, Streptococcus spp, etc
- Some gram negatives: H. pylori, E. coli, Yersinia enterocolitica, Proteus mirabilis
- Antiparasitic
- Candida spp

Usnea spp (Old Man’s Beard)

- Anti-inflammatory- in one study as or more effective as NSAID and hydrocortisone
- Anti-oxidant: activates superoxide dismutase (SOD) and glutathione transferase (GST) enzymes, protects against damage in mucosal cells
- Therapeutic Dose 10-15ml daily 1:2 extract


SIFO - small intestinal fungal overgrowth

- Large intestinal fungal overgrowth also very common
- Issues with candida spp:
  - Often cause similar symptoms to SIBO
  - Commonly forms biofilm
  - Overgrowth easily evades detection

Dr Rao study
- SIFO co-morbid with SIBO in 20%
- SIFO found in 26% of patients with “unexplained Gi symptoms”

Antifungal herbs

- Many of the herbs discussed also exhibit antifungal properties
- Classic antifungal herbs include Pau D’Arco, Uva Ursi, Berberine herbs
- Essential oils of clove, oregano, and thyme are particularly useful
- Oregano
- Horopito

**Oreganum vulgare (Oregano)**

- Traditionally used for digestive, urinary, and respiratory disorders.
- Carvacrol main active antimicrobial constituent (mainly antifungal)
- Active against candida spp, but also S. aureus, Pseudomonas a., and Blastocystis hominis
- Clinically shown to be effective for SIFO and methanogens
- Effective against candida biofilm
- Antioxidant
- Usually dosed as oil of oregano (50-100mg 2x daily)


**Pseudowintera colorata (Horopito)**

- Native to New Zealand
- Active constituent: Polygodial
- Strong antifungal activity against the yeast-like fungi C. albicans, C. utilis, C. kruzei, Cryptococcus neoformans, S. cerevisiae and also filamentous fungi including T. mentagrophytes, T. rubrum and Penicillium marneffei
- Moderate antibacterial activity against both gram-positive bacteria (including Bacillus subtilis and Staphylococcus aureus) and gram-negative bacteria (including Escherichia coli and Salmonella)
- MOA: polygodial is a nonionic surfactant that damages the permeability barrier of yeast cells.


**Polygodial**

Liquid antimicrobial formula

- SIBO formula- 7.5ml 2 x daily
  - Oregon grape (or Coptis/Goldenseal)
  - Pomegranate
  - Artemisia
  - Burr Marigold

- SIBO/SIFO formula - 7.5 ml 2 x daily
  - Pomegranate
  - Usnea
  - Horopito
  - Oregon grape (or Coptis/Goldenseal)
**Curcumin- anti inflammatory and antioxidant**

- Curcumin is one of the active constituents of Turmeric
- Widely studied herb with multiple applications
- Anti-inflammatory effect very well established, both in research and clinically
  - Inhibits NFkB, COX2, LOX, MAP, TNFa, PGE2
- stimulates the gallbladder to produce bile.
- The German Commission E, which determines which herbs can be safely prescribed in Germany, has approved turmeric for digestive problems. And one double-blind, placebo-controlled study found that turmeric reduced symptoms of bloating and gas in people suffering from indigestion.

**Curcumin in IBS**

- 2004 study of 207 randomized patients received either 1.8g or 3.6g of dried turmeric daily for 8 weeks
- “IBS prevalence decreased significantly in both groups between screening and baseline (41% and 57%), with a further significant drop of 53% and 60% between baseline and after treatment, in the one- and two-tablet groups respectively (p < 0.001). A post-study analysis revealed abdominal pain/discomfort score reduced significantly by 22% and 25% in the one- and two-tablet group respectively, the difference tending toward significance (p = 0.071). There were significant improvements in all bar one of the IBSQOL scales of between 5% and 36% in both groups, approximately two thirds of all subjects reported an improvement in symptoms after treatment, and there was a favorable shift in self-reported bowel pattern. There were no significant differences between groups”

**Herbal Prokinetics**

- Dr. J’s Herbal Bitters formula:
  - Oregon grape/Gentian/Baical Skullcap/Dandelion root: 2-3 whole droppers in water 15 min before meals
  - Dandelion root: cholagogue
  - Gentian, Oregon Grape: bitters stimulate HCL secretion, possibly motility
  - Baical skullcap: anti-inflammatory, antioxidant

- Formula IG - Iberis amara, Angelica archangelicacarum carvi, Silybum marianum, Melissa officinalis, chelidonium majus, Mentha piperitae, Glycerrhiza
  - 20 drops 3 x daily before meals and before bed. Or 60 drops at bed time

- Formula MP: Ginger, 5HTP, acetyl L carnitine, P5P, dose 3 caps morning and night
- Clove extract?

**GI Antispasmodics and Carminatives**

- Spasmolytics help with regulating motility and abdominal hypersensitivity

- Chamomile - also anxiolytic
  - a- bisabolol reduce visceral nociception
  - Apigenin - mild anxiolytic via benzodiazepine receptors, anti-inflammatory - inhibits IL-6 and TNF-a
  - Traditionally used for nervous diarrhea - binds to 5HT 4 receptors
  - 2-3 tsp of flowers per cup of tea to be taken TID ic
  - Tincture- 1-2ml TID pc
Carminatives - gas removal from GI tract

- Caraway seed - very effective carminative and spasmolytic
  - Active constituents: Carvol and d-limonene (carvone)
  - Relaxant effect on smooth muscle response to acetyl choline
  - Used as tea or in tincture
- Fennel
  - Fenchone and anethol

Carminative Tea - In equal parts:
- Caraway seeds
- Fennel seeds
- Anise seeds
- 1 teaspoon, crush seeds and steep for 20 minutes in 1 cup of water
- Drink after each meal

Parting Thoughts

- Use herbs before microbiome-disrupting antibiotics.
- Only use herbal medicines from reputable manufacturers who test batches frequently
- Herbs can be combined to make patient specific medicines
- Prescribe from professional brands only

Thank You