Botanicals, Biofilms, and Chronic Infections

PAUL BERGER
TRADITIONAL ROOTS HERBAL CONFERENCE
NATIONAL COLLEGE OF NATURAL MEDICINE
MAY 2016
PORTLAND, OR

Biofilms
Bacteria live in a biofilm state

**Planktonic form.** Free moving

**Biofilm form.** Non-mobile, linked in a matrix

The biofilm form of bacteria is resistant to both antibiotic therapy and the immune system. Most bacteria on the human body exist in biofilm form. Most are beneficial commensal bacteria and provide barrier, immune, and metabolic functions.

**Biofilms are part of normal microbiome defense of the body but pathological biofilms are nearly universally present in:**

- Oral plaque, periodontal disease, abscess
- MRSA infections on skin
- Other skin infections
- Chronic wounds and ulcers
- Chronic sinus infection
- Upper GI disturbances
- Vaginal infection
- Bladder infection

**Biofilms**

![THE FORMATION OF A BIOFILM]

- **Attachment:** Bacteria adhere to a surface in a mass called a biofilm. A non-soluble matrix is secreted. It travels into the body's internal fluids.
- **Expansion:** The cells grow and divide, forming a complex filamentous chain. The bacterial cells attach to each other and secrete a matrix. More cells attach to the chain to form a continuous cell mass.
- **Maturation:** The cells secrete a matrix that helps the biofilm attach to the surface. The biofilm becomes more stable and resistant to environmental factors such as antibiotics. The biofilm also becomes more resistant to mechanical forces, allowing it to withstand the body's defenses.
- **Resistance:** The biofilm resists detachment from the surface, making it difficult to remove. The biofilm can also limit the diffusion of antibiotics and immune cells, making it more resistant to treatment.
Biofilms are the normal life state for bacteria and some fungi.

- Biofilms can be viewed as semi-independent multicellular organisms with specialized metabolism and immune defenses.
- They are interlinked by filaments of polysaccharide, protein, or strands of genetic material.
- A gradient of metabolism from aerobic at the surface to anaerobic at the core develops, allowing resistance to substances which might affect the metabolism.
- In some species, an attached biofilm layer provides nutrients to a superficial layer, which may secrete antibiotics, reproduce, etc.
- Once aggregated, bacteria in biofilms can dramatically change their functions and secretions.
Biofilms have not been studied in the living organism. Biofilms in infected wounds are typically in the range of 5 to 10 micrometers, or 1/100 of a millimeter. Requires about 100x magnification to be visible.

One sample of Borrelia biofilm in tissue samples required 400X magnification.
Killed cells in the biofilm are red. Colistin* kills the anaerobes at the center of the biofilm, but leaves the metabolically active aerobes at the surface intact, and the biofilm is completely restored. Tobramycin kills the aerobes, but leaves the anaerobes intact. The combination can kill the biofilm.

* nephrotoxic last resort antibiotic used in Cystic Fibrosis infections
Multispecies biofilms

Microorganism biofilms frequently form, which may also include fungi.

Below: Oral plaque is a multispecies biofilm with constantly changing and evolving components.

Tolerance genes are most easily spread in multispecies biofilms. Multispecies biofilms evolve in their composition and their resistance with each dose of antibiotics.

Right: A 3 species biofilm grown in saliva.

Below: A “corn cob” biofilm with cocci attached to bacilli.
Bacterial vaginosis multispecies biofilm

"Currently, it is consensus that BV involves the presence of a dense, structured and polymicrobial biofilm, primarily constituted by G. vaginalis clusters, strongly adhered to the vaginal epithelium."

Berberine and companion alkaloids

May act against biofilms by attacking both aerobes and anaerobes.

In this ex vivo trial both Coptis root and its constituent berberine significantly inhibit the growth of gut bacteria under both aerobic and anaerobic conditions in vitro. In vivo, both RC and berberine significantly inhibit the growth of Firmicutes under anaerobic conditions.
The Odwalla Juice E.coli epidemic

- Odwalla juice marketing unpasteurized juices during the 1990s.
- In 1996, a batch of their apple juice became infected with pathogenic E.coli bacteria. The apple juice is a component in most of their juices.
- An epidemic followed across the American West, with cases reported in Washington State, Colorado, and California. One child died in Colorado, and 13 more were hospitalized with kidney damage.
- A number of individuals in Boulder, CO became sick. None were ever recorded in the official statistics of the epidemic.
- A tincture formula of equal parts of Hydrastis, Mahonia, Berberis, and Coptis proved rapidly effective against a case with fever and bloody diarrhea (blood resolved after two moderate doses).

Alkaloids in some berberine-containing plants.

Most of these alkaloids have antimicrobial or other pharmacological effects in scientific trials.

<table>
<thead>
<tr>
<th>Alkaloid</th>
<th>Formula</th>
<th>Toxicity</th>
<th>Berberine</th>
<th>Coptis</th>
<th>Hydrastis</th>
<th>Mahonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berberine</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrastine</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berbamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Berberastine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Canadine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Columbine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coptisine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epiberberine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrastinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Jatrorrhizine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxicanthine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxyacanthine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palmatine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrahydroberberastine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Potential synergistic alkaloids from Hydrastis, Mahonia, Berberis, and Coptis combination

New alkaloids with each addition are marked **bold** italic.

The possible synergistic auxiliary compounds in each plant may also be present.

Berberine compound formula
Berberine and its related alkaloids common in berberine-containing plants each inhibit bacteria individually.

Disabling Microbial Defenses

This Biofilm will now come to order “Quorum sensing” by bacteria

- planktonic bacteria secrete signaling molecules
- As the population grows, the concentration of signaling molecules rises, and binds to surface receptors on the bacteria.
- This triggers bacterial DNA transcription.
- Expression of matrix material to form biofilm.
- Production of antibiotics to protect the colony from other bacteria, fungi, etc.
- Production of adhesion molecules.
- Production of proteases and other substances enabling invasion of tissues.

PUBMED search: (biofilm* OR quorum)
Some plants with anti-biofilm/quorum properties

- The discovery of the quorum-sensing property essential to formation and functioning of a biofilm has led to a research quest for plant constituents with anti-quorum or anti-biofilm properties.

**Science + tradition**
- Allium
- Hydrastis (leaf)
- Commiphora myrrha
- Boswellia
- Achillea
- Aloe
- Hypericum
- Althea
- Arctostaphylos
- Acalypha
- Quercus and tannins

**Traditional use**
- Anemopsis
- Larrea
- Baptisia
- Thuja
- Bursera

Multiple Drug Resistant Efflux Pumps (MDR)

- Bacteria contain transporters in their membranes which actively pump harmful substances back out of the cell.
- The process is non-specific, evicting a wide variety of substances. It can result in complete inactivation of antibiotic substances.
- MDR activity is responsible for bacterial resistance to both plant and pharmaceutical antibiotics.
- A bacterial population will evolve to contain robust MDR pump activity in response to plant or pharmaceutical antibiotics.
- Bacteria of unrelated species can acquire the MDR pump resistance genes from each other.
- The pharmaceutical quest for effective MDR pump inhibitors (MDRi) has led to a flurry of research into plant compounds in the last few years.

Efflux pumps

- Efflux pumps allow microorganisms to expel many kinds of substances harmful to them.
- Genes coding for more efficient efflux pumps are part of bacterial resistance.
- Efflux pump inhibition is a potential target for antimicrobial therapy with plants or drugs.
MDR pump inhibitors in plants

- Most isolated plant antimicrobial substances are not effective against gram-negative bacteria, due to membrane functions and MDR pumps, but the plants themselves may be very effective due to synergistic constituents, including MDR inhibitors.
- Addition of MDR constituents can multiply effectiveness dramatically 100-1000x.
- Many whole plants contain MDR pump inhibitors.
- Likewise, plant material rich in MDR pump inhibitors may be added in formula to topical preparations or other herbs.

Some widely dispersed MDRI constituents

<table>
<thead>
<tr>
<th>Luteolin</th>
<th>Apigenin</th>
<th>Kaempferol</th>
<th>Myricetin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artemisia</td>
<td>Artemisia</td>
<td>Allium</td>
<td>Arctostaphylos spp.</td>
</tr>
<tr>
<td>Echinacea</td>
<td>Echinacea</td>
<td>Echinacea</td>
<td>Arbutus spp.</td>
</tr>
<tr>
<td>Plantago</td>
<td>Plantago</td>
<td>Althaea</td>
<td>Other Ericaceous</td>
</tr>
<tr>
<td>Baptisia</td>
<td>Baptisia</td>
<td>Althaea</td>
<td>Other Ericaceous</td>
</tr>
<tr>
<td>Luteolin</td>
<td>Luteolin</td>
<td>Luteolin</td>
<td>Luteolin</td>
</tr>
<tr>
<td>Apigenin</td>
<td>Apigenin</td>
<td>Apigenin</td>
<td>Apigenin</td>
</tr>
<tr>
<td>Kaempferol</td>
<td>Kaempferol</td>
<td>Kaempferol</td>
<td>Kaempferol</td>
</tr>
<tr>
<td>Myricetin</td>
<td>Myricetin</td>
<td>Myricetin</td>
<td>Myricetin</td>
</tr>
</tbody>
</table>

Some plants containing MDRI

- Hypericin (leaf)
- Some Berberis species (leaf)
- Allium sativum
- Allium spp.
- Calendula
- Plantago
- Echinacea
- Artemisia spp.
Plants and biofilms

Plants can do through multiple mechanisms what no drug can do.

Many plants have developed mechanisms to kill bacteria, prevent or disrupt quorum-sensing in bacteria, or suppress efflux pumps. This is essential to their survival. Synergistic constituents in a single plant may:

- Attack microbial cell wall
- Attack microbial metabolism
- Disrupt bacterial resistance functions (MDR pumps for instance)
- Disrupt quorum sensing
- Disrupt the functions triggered by quorum sensing
- In humans, they may also stimulate local host resistance or circulation

Hydrastis leaf

- Contains all the Hydrastis alkaloids but in lower concentration than the root
- Contains at least 3 MDRi which effectively double the potency of berberine
- Also contains anti-quorum and anti-biofilm properties unrelated to its alkaloids
- Sustainably grown Hydrastis leaf may be added to formulas to almost any topical antimicrobial to improve results

Host defense against biofilms
In the host response to chronic biofilms, the cellular components normally present only during the acute phase of the innate immune system are chronically activated, especially Polymorphonuclear leukocytes (PMNs). This chronic activation of an acute response can result in tissue inflammation and damage.

PMNs: Neutrophils, Eosinophils, Basophils, Mast Cells

Polymorphonuclear leukocytes (PMN)

The biofilm protects bacteria from otherwise bactericidal PMNs. Oxidative bursts from the PMN damage the tissues around the biofilm and produce inflammation.
PMN stained in blue surround the biofilm. Their oxidative bursts can damage tissues.

Damage-response model of infection

Examples of host damage

- Non-healing wounds and ulcers. Immune response damages tissues.
- Tuberculosis. Damage to lung by immune response.
- Chronic viral hepatitis. Damage to liver by immune response.
- HIV infection triggering autoimmune response
- Chronic Lyme infection. Damage to connective tissues by response.
- Possible chronic infection triggered autoimmunity
- Permanent presence of high volumes of antigenic food substances produce systemic inflammation.

The “Biofilm Complex”

- Planctomic microorganisms
- Microorganisms in a biofilm matrix
- Microorganisms actively resisting antimicrobial substances through efflux pumps.
- A continuous and ongoing evolution of resistance to host and antimicrobials.
- Damage to the tissues through invasion or toxins
- An ineffective active immune response which may further damage the tissues
- Non-resolving inflammation

A Plant Constituent-Synergy model of therapeutics for the chronic biofilm complex
Damage-response therapeutics
A synergy model for multi-constituent topical applications

<table>
<thead>
<tr>
<th>Antimicrobial Effects</th>
<th>Enhance Immunity</th>
<th>Reduce damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct antimicrobial effects</td>
<td>Increase local circulation</td>
<td>Reduce local inflammation</td>
</tr>
<tr>
<td>MOD pump inhibition</td>
<td>Enhance local immunity</td>
<td>Local tissue damage</td>
</tr>
</tbody>
</table>

These properties are all possessed by some single plants, and with some simple plant combinations.

Direct applications

- The plant material or its extract comes in direct contact with the cell and its environment.
- All of the plant constituents can come directly into contact with tissue in high concentration, and can act synergistically.
- Significance for large molecules, essential oils.
- Plants may be combined for multiple effects
- Plants may be delivered in media with anti-biofilm effects
- May apply to external skin, throat, ear, sinuses, stomach, vagina, and some constituents may be delivered through the urinary tract.

Potential synergistic actions against the biofilm complex

<table>
<thead>
<tr>
<th>Plaese</th>
<th>Inflammatory</th>
<th>Vulnerary</th>
<th>Antiprinqu</th>
<th>Anti-biofilm</th>
<th>FD</th>
<th>Local Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calendula</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Plantago</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hypericum</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Echinacea</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Althaea</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Infused oil: Olive oil also has wound healing and anti-inflammatory effects.

Echinacea wash from decoction of 1 ounce per liter for 40 minutes.

Echinacea wash from tincture 1 part Echinacea to 3-4 parts water.
Herbs with synergistic effects against biofilms

|      | Anti-
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Septic</td>
</tr>
<tr>
<td></td>
<td>Immune</td>
</tr>
<tr>
<td></td>
<td>Anti-Biofilm</td>
</tr>
<tr>
<td></td>
<td>MRDi</td>
</tr>
<tr>
<td>Lamina</td>
<td>x</td>
</tr>
<tr>
<td>Thuja</td>
<td>x</td>
</tr>
<tr>
<td>Anemopsis</td>
<td>x</td>
</tr>
<tr>
<td>Baptisia</td>
<td>x</td>
</tr>
<tr>
<td>Hypericum</td>
<td>x</td>
</tr>
<tr>
<td>Althaea</td>
<td>x</td>
</tr>
</tbody>
</table>

Stimulate local circulation

|      | Stimulated | Anti-
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Septic</td>
</tr>
<tr>
<td></td>
<td>Immunity</td>
</tr>
<tr>
<td></td>
<td>Anti-Biofilm</td>
</tr>
<tr>
<td></td>
<td>MRDi</td>
</tr>
<tr>
<td>Thuja</td>
<td>x</td>
</tr>
<tr>
<td>Myrica</td>
<td>x</td>
</tr>
<tr>
<td>Baptisia</td>
<td>x</td>
</tr>
<tr>
<td>Commiphora</td>
<td>x</td>
</tr>
<tr>
<td>Achillea</td>
<td>x</td>
</tr>
<tr>
<td>Capsicum</td>
<td>x</td>
</tr>
</tbody>
</table>

Some historical combinations
Garden variety infused topical oil

<table>
<thead>
<tr>
<th>Plant</th>
<th>Anti-inflammatory</th>
<th>Vulnary</th>
<th>Antiseptic</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDRi</th>
<th>Local Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calendula</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Plantago</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hypericum</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

- "Rheumatic drops" taken internally, topical antiseptic, throat spray
- Externally: "the most powerful antiseptic known, and is on that account highly serviceable in all putrid affections whatever"
- Used as surgical disinfectant with simultaneous internal immune stimulation by the later Physiomedicalists (post germ theory)
- RS Clymer later recommended substitution of Echinacea for Capsicum in the formula. Can use all three in suitable proportions

Samuel Thomson’s Number Six

<table>
<thead>
<tr>
<th>Plant</th>
<th>Stimulant</th>
<th>Anti-Inflammation</th>
<th>Antiseptic</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDRi</th>
<th>Vulnary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commiphora</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Capsicum</td>
<td>xxx</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Echinacea</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

A classical pair

<table>
<thead>
<tr>
<th>Plant</th>
<th>Stimulant</th>
<th>Anti-Inflammatory</th>
<th>Antiseptic</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDRi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrastis</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Myrrh</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Traditionally used for oral infections and non-healing wounds
Hydrastis and Myrrh

- Topical wash for infection
- Antibacterial, antiviral, antifungal
- Spray for sore throat
- Gum disease
- Topical for gastric mucosa
- Powerful systemic effects (mucous membrane tonic, general alterative and tonic, antimicrobial through separate mechanisms, in low dose is balanced warm, cold, moist and dry.

Sinusitis spray

- Get a 2 ounce sinus spray bottle
- Add 1 teaspoon of glycerine. Not more.
- Add 15 drops each of Hydrastis and Myrrh*. Not more.
- Fill to 2 oz with water.
- Spray into sinuses up to 4 times per day.
- Frequently will clear chronic sinusitis within 4 days.

*Original recipe called for 30 drops of Anemopsis

Possible combination

<table>
<thead>
<tr>
<th>Stimulant</th>
<th>Anti-inflammatory</th>
<th>Antiseptic</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Larrea</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
Esberitox

- Developed in Europe for internal use as an immune stimulant.
- A very potent potential topical treatment. Prepare as decoction.
- Note traditional use of Baptisia was primarily external application of the tea.

<table>
<thead>
<tr>
<th></th>
<th>Stimulant</th>
<th>Anti-inflammation</th>
<th>Vulnerary</th>
<th>Anti-biofilm</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echinacea</td>
<td>cold</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Baptisia</td>
<td>cool</td>
<td>x</td>
<td>-</td>
<td>-</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Thuja</td>
<td>warm</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Roberts formula for ulcers

- Helicobacter pylori is a normal component of the gastric microbiome. In some cases it is the dominant species.
- It normally grows in a biofilm separated from the mucosa by a mucous layer. Pathology may be due to loss of the mucous layer.
- For a complete discussion of H pylori, the history of its discovery, and subsequent discovery of systemic harms that can result from it eradication, see Missing Microbes by Glaser.
- Roberts formula for ulcers was developed mid 20th century, long before the possible infectious basis of gastric ulcers was known, and before the discovery of H pylori. Most of the herbs are those that would traditionally be used on topical ulcers or poorly healing wounds. Later in the 20th century, J. Bastyr added Baptisia and several other components to the formula.

Roberts Formula for Ulcers

<table>
<thead>
<tr>
<th></th>
<th>Antibiotic</th>
<th>Anti-inflammation</th>
<th>MDR</th>
<th>Local immunity</th>
<th>Anti-biofilm</th>
<th>Vulnerary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Althaea</td>
<td>cool</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Geranium (crataegus)</td>
<td>cold</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hydrastis (leaf)</td>
<td>cool</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echinacea</td>
<td>cool</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Phytolacca</td>
<td>cold</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Baptisia</td>
<td>cool</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

*Specific strong activity against H. pylori

5/19/2016
Acalypha spp. Yerba del Cancer.
A universal folk remedy for wounds in Mexico

Acalypha phleoides (syn. lindheimeri)

A. californica

Michael Moore: “For chronic infections when nothing else has worked.”

Acalypha and Arctostaphylos

Acalypha (AJ) is a relatively poor antimicrobial.
Arctostaphylos u. (AU) is very strong.

Of 25 Mexican plants tested, Acalypha and Uva ursi were #1 and #2 in one measurement of anti-quorum activity. Most had no activity.
In another measure of quorum sensing activity, Acalypha was #1 of the 25.

Anti-microbial and anti-biofilm effects of Uva Ursi


Quercus species
Constituent synergy for anti-quorum properties

- Dried then rehydrated Quercus bark
- The whole plant had mild anti-microbial but very strong anti-quorum sensing activity
- Ten constituents tested individually
- Two of ten showed anti-microbial and anti-quorum activity
- Five more showed anti-quorum activity without anti-microbial activity
- Only a recombination of all constituents together showed activity equal to the whole plant.

Allium sativum

- Raw fresh cut garlic contains high amounts of allicin, which has broad-spectrum antimicrobial and anti-biofilm effects.
- Allicin breaks down rapidly once garlic is cut or crushed. Breakdown products have anti-biofilm and antimicrobial effects.
- The constituent ajoene, which is abundant in oil-infused garlic preparations, has a potent anti-biofilm effect.
- Some of these non-allicin constituents may be delivered to a biofilm after oral ingestion.
- Fresh garlic can produce second and third degree in burns.

Allium sativum applications

- Two cloves (not whole bulbs) in liter of water, blended and strained through cheesecloth.
- Poultice
- Foot bath or hand bath
- Mouthwash for thrush
- Douche
- Infused oil for ear

Media
Vinegar and biofilms

- Acetic acid has an anti-microbial effect against established biofilms both in vitro and in open wounds.
- It is effective at 100% eradication of established P. aeruginosa and S. aureus at a concentration of 1% acetic acid.
- The anti-biofilm effect is not due to pH value of the bacteria, because HCl at the same pH has no effect.
- The effect is due to the acetic acid molecule itself.
- Application six times a day for twenty minutes on non-healing diabetic ulcers. (See following slides)

Day 0 vs Day 11 of antibiotic resistant diabetic foot ulcer treated with vinegar. Note complete lack of suppuration.

Days 0, 3, and 6 of vinegar treated antibiotic resistant diabetic foot ulcers. Note disappearance of suppuration and appearance of circulation by day 3.
Treatment of a year-long antibiotic resistance diabetic foot ulcer with vinegar. Days 0 and 6. See method of application in middle slide.

Stages of chronic ulcers

Antibiotic treatment results in resistance, evolution of the biofilm, and ultimately to co-infection by additional species and yeasts (purple circles) in multispecies biofilms.
Honey

- Honey in a dilution of 1/2 was tested against planktonic and biofilm forms of antibiotic-resistant P. aeruginosa and E. coli.
- Tested honey was Manuka honey, which may contain antimicrobial volatile substances. Some Canadian honey samples were ineffective.
- The honey completely eradicated planktonic forms and reduced biofilm forms of both bacteria by 63-91%.


Oral biofilms

- A healthy microbiome may exist in the biofilm on the teeth.
- Sugars drive evolution of the biofilm on the teeth toward acid-producing bacteria and caries.
- Poor hygiene results in evolution of the multispecies biofilm of anaerobes which can live under the gum line. Subsequent inflammation is destructive to the tissues.
- Anaerobes may spread through virulent planktonic bacteria to other areas of the body, to medical implants, kidney stones, atherosclerotic plaque, etc.

Treatments for oral infection

- Combinations of Hydrastis and Myrrh, applied generously, diligently, and persistently have saved teeth that were due to be pulled because of severe gum disease. Consider Hydrastis leaf.
- May also work with powdered Myrrh and sea salt.
- Will not work without first mechanical cleaning of the teeth.
- Abscesses or infected root canals cannot be addressed with herbs.
- Strong Echinacea tea internally, and also held as a mouthwash, have effectively prevented oral infections following gum surgery when antibiotics were refused.
- Also effective internally in a case study of facial cellulitis following root canal, when antibiotics were refused.
Tooth powder
For treatment or maintenance after cleaning

<table>
<thead>
<tr>
<th>Part</th>
<th>Stimulant</th>
<th>Anti-inflammatory</th>
<th>Antiseptic</th>
<th>Immune</th>
<th>Biofilm</th>
<th>MDRi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quercus</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Myrrh</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Myrica</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hydrastis</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Cinnamomum</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

This is a formula from Candis Cantin Kriage

Bacterial vaginosis

- The normal biome of the vagina is dominated by one of several vagina-specific Lactobacillus species.
- BV is characterized by strongly tissue-adherent multispecies biofilms constructed on a dominant Gardnerella matrix.
- Antibiotics are ineffective because of the biofilm, and because restoration of the vaginal specific Lactobacillus is necessary.
- The general pattern of therapy is:
  - Keep the environment acidic
  - Apply probiotics of vaginal-specific lactobacillus.
  - Apply topical therapeutics with antimicrobial and anti-biofilm effects

Some traditional treatments

- Vinegar douches. May have anti-biofilm effects independent of pH effects.
- Boric acid capsules, BID. Boron may have anti-biofilm effects independent of pH.
- Boric acid mixed with powder of Hydrastis, Mahonia, or Berberis. Might be enhanced by the use of leaf of Hydrastis or Mahonia.
- Douches of Hydrastis tea. Consider adding the leaf, with the entire berberine compound formula.
- Douches of Allium sativum. Must strain the blended preparation through cheesecloth to prevent skin irritation (garlic can cause burns).
Boric acid and biofilm formation

Beneficial effects in BV may be due to the effect of the Boron molecule on biofilm formation rather than to the acidity.


Garlic vs Flagyl for Bacterial Vaginosis

- 500 mg powder of Allium sativum
- 250 mg Metronidazole
- Two tablets with meals every 12 hrs.
- Successful application with reduction of the biofilm model that the anti-microbial and possibly the anti-biofilm constituents are delivered systemically to the vaginal mucosa.


Internal biofilms

- These usually require mechanical assistance to remove.
- High doses of single antibiotics are ineffective.
- High dose antibiotic combinations may be effective.
- Tooth abscess
- Medical devices and implants
- Tissue fillers
- Chronic tissue infection (Borreliosis)
Borrelia biofilms in vitro and in vivo

Borrelia biofilms in vitro are large enough to be seen with the naked eye. In human tissue, the samples above were visible only at 40x magnification.