Cosmesceuticals: Botanicals

Gail Humble, MD

The following potential conflict of interest relationships are germane to my presentation.

Speaker’s Bureau, Clinical Investigator: Sanofi Aventis, Merz Pharmaceutical, Stiefel Labs

Botanicals
Botanicals

- Plant extracts from leaves, roots, fruits, berries, stems, twigs, barks, and flowers
- Unregulated category of ingredients
- Consist of 2 or more cellular process to treat/prevent disease known as secondary metabolites

Botanical Formulation Considerations

- Plant source
  - Leaves, roots, berries, fruits, stems, twigs, barks, flowers
- Growing conditions
  - Soil composition
  - Amount of available water
  - Climate variations
  - Plant stress

- Harvesting conditions
  - Time from harvest to transport
  - Care of plant materials during shipping
  - Storage conditions prior to manufacture
- Preparation method
  - Crushing, grinding, boiling, distilling, pressing, drying
**Botanical Formulation Considerations**

- Final extract status
  - Liquid, powder, paste, syrup, crystal
- Concentration
  - Sufficient amount of activity to produce biologic effect

**Botanical Classifications**

- Antioxidants
- Anti-inflammatory
- Skin-soothing agents

**Antioxidant Botanicals**

- Quench singlet oxygen and reactive oxygen species
- Can be classified as flavonoids, carotenoids, polyphenols
- Largest source of botanical antioxidants is food
**Nutritionally Derived Botanical Antioxidants**

- Rutin (apples, blueberries)  flavone
- Quercetin (apples, blueberries)  flavone
- Hesperedin (lemons, oranges)  flavone
- Diosmin (lemons, oranges)  flavone
- Mangiferin (mango)  xanthone
- Mangoïsin (bilberry)  xanthone
- Astaxanthin (tomatoes)  carotenoid
- Lutein (tomatoes)  carotenoid
- Lycopene (tomatoes)  carotenoid
- Rosmarinic acid (rosemary)  polyphenol
- Hypericin (St. John’s wort)  polyphenol
- Ellagic acid (pomegranate)  polyphenol
- Chlorogenic acid (blueberry leaf)  polyphenol
- Oleuropein (olive leaf)  polyphenol

**Soy**

- Species name: Glycine max
- Source of antioxidant flavonoids, genistein and daidzein
- Phytoestrogen
- Increases skin thickness and promotes collagen synthesis
- Genistein quenches peroxyl radicals and protects against lipid peroxidation

**Soy: Mechanism of Action**

- Collagen synthesis
- Stimulates elastin synthesis
- Photoprotectant
- Anti-inflammatory
- Antioxidant
- Anti-proliferative
- Antitumor
- Barrier repair
- Treats extrinsic aging
- Treats hyperpigmentation
<table>
<thead>
<tr>
<th>Soy Secondary Metabolites</th>
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<tbody>
<tr>
<td>• Phosphatidylinoline</td>
</tr>
<tr>
<td>• EFA</td>
</tr>
<tr>
<td>• Isoflavones (genistein,</td>
</tr>
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<td>daidzein)</td>
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<td>• STI</td>
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<tr>
<td>• BBI</td>
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<td>• Saponins</td>
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<tr>
<td>• Vitamin E</td>
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<tr>
<td>• Phytosterols</td>
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<td>• Phytoestrogens</td>
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<td>• Proteases</td>
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<table>
<thead>
<tr>
<th>Curcumin</th>
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<tbody>
<tr>
<td>• Polyphenol antioxidant</td>
</tr>
<tr>
<td>derived from turmeric</td>
</tr>
<tr>
<td>root</td>
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<tr>
<td>• Provides skin related</td>
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<tr>
<td>antioxidant benefits</td>
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<tr>
<td>• Used in Asian medicine</td>
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<tr>
<td>for a variety of skin</td>
</tr>
<tr>
<td>conditions (bruising,</td>
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<tr>
<td>ulcers, fungal infections)</td>
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<table>
<thead>
<tr>
<th>Curcumin: Mechanisms</th>
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<tbody>
<tr>
<td>of Action</td>
</tr>
<tr>
<td>• Collagen synthesis</td>
</tr>
<tr>
<td>stimulant</td>
</tr>
<tr>
<td>• Treats extrinsic aging</td>
</tr>
<tr>
<td>• Immune stimulating</td>
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<tr>
<td>• Antimicrobial</td>
</tr>
<tr>
<td>• Anti-inflammatory</td>
</tr>
<tr>
<td>• Antioxidant</td>
</tr>
<tr>
<td>• Antitumor</td>
</tr>
<tr>
<td>• Chemoprotective</td>
</tr>
<tr>
<td>• Stimulates epidermal</td>
</tr>
<tr>
<td>proliferation</td>
</tr>
<tr>
<td>• Estrogenic</td>
</tr>
<tr>
<td>• Wound healing</td>
</tr>
<tr>
<td>• Treats radiodermatitis</td>
</tr>
<tr>
<td>• Treats scabies</td>
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</tbody>
</table>
**Curcumin: Active Secondary Metabolites**

- Tumerone oil
- Curcuminoids

**Silymarin**

- Extract of silbum marianum (milk thistle plant)
- Three flavonoids derived
  - Silybin
  - Silydianin
  - Silychristine
- Prevents lipid peroxidation

**Silymarin: Mechanisms of Action**

- Anti-inflammatory
- Antioxidant
- Antitumor
- Chemoprotective
- Treats rosacea
- Photoprotective
Silymarin: Active Secondary Metabolites

- Flavonoid
- Silybin

Silymarin Clinical Studies

- No trials for extrinsic aging
- Topical silymarin reduced 92% UVB-induced skin tumors in mice

Pycnogenol

- Extract of French marine pine bark (Pinus pinaster)
- Water soluble compound containing phenolic compounds, ferrulic acid
- Free radical scavenger returning vitamin C to its active form
**Pycnogenol: Mechanisms of Action**
- Anti-inflammatory
- Antioxidant
- Antitumor
- Photoprotective
- Wound healing
- Chemopreventive
- Treats hyperpigmentation

**Pycnogenol: Active Secondary Metabolites**
- Procyanidins
- Catechins
- Flavonoids

**Pycnogenol Clinical Studies**
- No trials for extrinsic aging
- Open label 30 females with melasma treated for 30 days showing highly statistically significant improvement in melasma and pigment intensity compared to baseline

www.naturaldatabase.com
Citric Acid

- Astringent and antioxidant properties
- Derived from citrus fruits
- Can be used as a preservative with low sensitizing potential

Grape Seed Extract

- Vitis vinifera
- Consists of various compounds (flavonoids, tannins, stilbenes)
- Dlignomeric proanthocyanidins-potent antioxidant, anti-inflammatory, antihistaminic, anticarcinogenic properties
- Stabilize elastin, collagen, ground substance
- Improves photoaging, reduces edema

Grape Seed Extract: Active Secondary Metabolites

- Polyphenol flavonoids (proanthocyanidins)
- Linoleic acid
- Resveratrol
Grape Seed Extract Clinical Studies

- Taken orally for 6 months, grape seed significantly reduced melasma in Japanese women
- Melanin index significantly reduced

Pomegranate

- Punica granatum
- More potent antioxidant than grape seed extract
- Comprised of ellagic acid, ascorbic acid, niacin, alkaloids

Pomegranate Mechanisms of Action

- Anti-inflammatory
- Antioxidant
- Cyclo-oxygenase inhibitor
- Inhibits prostaglandin synthesis
- Chemopreventive
- Photoprotective
- Stimulates epidermal proliferation
- Treats extrinsic aging
- Barrier repair
- Elastin synthesis stimulant
Pomegranate: Active Secondary Metabolites

- Antioxidant > green tea
- Ellagic acid
- Polyphenols
- Alkaloids

Mangosteen

- Exotic fruit found in Southeast Asia from Garcinia Mangostana tree
- Contains high antioxidant concentration in form of xanthones
- Has antioxidant, antibacterial, and anti-inflammatory effect
- Shown anecdotally to reduce hyperpigmentation, fine lines, rosacea, and acne when used topically

Anti-Inflammatory Botanicals
Ginkgo Biloba

• Contains polyphenols possessing anti-inflammatory effects
• Induce fibroblast formation via antiradical and anti-lipoperoxidant effects

Ginkgo Biloba Mechanisms of Action

• Antioxidant
• Anti-inflammatory
• Treats extrinsic aging
• Treats rosacea
• Treats vitiligo
• Chilbain therapy
• Elastin synthesis stimulant

Ginkgo Biloba: Active Secondary Metabolites

• Glcosides
• Terpines
• Flavonoids (quercetin)
**Ginkgo Biloba Clinical Studies**

- 25 patients suffering from vitiligo treated with 40 mg ginkgo biloba 3 times daily compared to 22 placebo treated patients in double-blind trial for 6 months
- Disease flaring ceased in 20 out of 25 in ginkgo group
- 50% or treated group had >75% repigmentation


**Green Tea**

- Contains flavonoids with endogenous antioxidant properties
- Also antibacterial and anti-inflammatory properties
- Demonstrated ability to postpone onset of cancer and heart disease clinically
- Studies show topically applied green tea reduced UVB-induced inflammation

**Green Tea: Mechanisms of Action**

- Treats extrinsic aging
- Antimicrobial
- Anti-proliferative
- Photoprotective
- Antitumor
- COX-2 inhibitor
- Chemopreventive
- Increases apoptosis
- Wound healing
- Treats rosacea
- Anti-inflammatory
- Antioxidant
Green Tea: Active Secondary Metabolites

- Polyphenols
- Flavonoids
- Quercetin
- EGCG
- Catechins
- Phenols
- Caffeine

Feverfew (Tanacetum parthenium)

- Potent anti-inflammatory, antioxidant, and anti-irritant properties
- Purified extract developed to minimize skin sensitization

Feverfew Anti-Inflammatory Properties

- Inhibition of proinflammatory cytokines release from activated lymphocytes
- Reduce neutrophil chemotaxis
- Inhibition of adhesion molecule expression
- Decrease in NK-K B-dependent gene transcription
Feverfew Clinical Study

- In study evaluating ability to inhibit TNFα release, purified feverfew extract demonstrated greatest inhibitory effect compared with numerous botanical compounds
- Purified feverfew extract inhibited TNFα release by factors or 35-fold to more than 1000-fold

Martin K et al. Poster presented 63rd AAD; Feb 2005; New Orleans, LA

Feverfew Clinical Studies

- 31 females with sensitive skin in 3 week randomized study were treated twice daily with feverfew
- Statistically significant reduction in redness, roughness, and irritation at one, two, three weeks
- Panelists saw statistically significant visible improvement at same time points

Tierney N et al. Daily use of a topical formulation containing parthenolide-free extract of feverfew clinically reduces the...

Skin Soothing Botanicals
Prickly Pear

- Plant contains water, sucrose, tartaric acid, citrus acid, and mucopolysaccharides
- Acts as sunscreen and moisturizer
- Protective coating over wounded skin

Aloe Vera

- Species name: A. barbendensis
- Colorless gel from plant contains water, mucopolysaccharides, amino acids, hydroxy quinone glycosides, minerals
- Should be present at 10% concentrations to have moisturizing effect

Aloe Vera: Mechanisms of Action

- Antioxidant
- Analgesic
- Anti-inflammatory
- Treats rosacea
- Treats psoriasis
- Wound healing
**Aloe Vera: Active Secondary Metabolites**

- Salicylates
- Magnesium
- Lactate
- Polysaccharides
- Mucilage

**Aloe Vera: Clinical Studies**

- 60 patients suffering from psoriasis were treated 5 days/week for 4 weeks with 0.5% aloe vera cream
- Statistically significant 83% cleared lesions vs. 8% placebo


**Allantoin**

- Derived from comfrey root
- Induces cellular proliferation
- Aids healing
- Has debriding effect, clearing necrotic tissue
**Witch Hazel**

- *Hamamelis virginiana*
- Most commonly used as an astringent
- Astringent action due to tannin content
- Plant tannins act as vasoconstrictors

**Witch Hazel: Mechanisms of Action**

- Anti-inflammatory
- Antimicrobial
- Astringent
- Antioxidant
- Elastin synthesis stimulant

**Witch Hazel: Active Secondary Metabolites**

- Tannins
- Gallic acid
- Quercetin
Witch Hazel Clinical Studies

- Reduced inflammation and pruritis in 36 atopic dermatitis patients
- Less effective in reducing UV-induced erythema than 1% hydrocortisone

Papaya

- Carica papaya
- Rich papain
- Papain is a proteolytic enzyme used in wound healing, resolution of bruises and scars

Papaya Mechanisms of Action

- Antimicrobial
- Antioxidant
- Inhibits arachidonic metabolism
- Anti-inflammatory
- Immune stimulating
- Increases lymphocyte counts
Papaya: Active Secondary Metabolites

- Papain
- Carpain enzymes
- Active elements
  - Caricin
  - Myrosin
  - Peptidase
  - Vitamins C & E

Miscellaneous Herbs & Botanicals

Echinacea

- Three species
- Contain polysaccharides, glycoproteins, flavonoids, caffeic and ferrulic acid derivatives, alkamides, alkaloids
- Stimulate immunity, protect collagen, antioxidant activity
- Effective in treating burns, infected lesions, psoriasis, photoaging, decubitis ulcers

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Garlic

- Allium sativum
- Action due to alkylcysteine sulfoxides
- Also composed of polysaccharides, saponins, vitamins A, B, C
- Possesses potent antimicrobial and antioxidative activity; stimulates immunity
- Beneficial in treating premature aging

Garlic: Mechanisms of Action

- Antimicrobial
- Antitumor
- Immune stimulating
- Antioxidant
- Enhances killer T-cells

Garlic: Active Secondary Metabolites

- S-allyl-2-cysteine organosulfurs
  - Allicin
  - Ajoene
- Saponins
- Polysaccharides
**Saw Palmetto**

- *Serenoa repens*
- Composed of sitosteroids, glucosides, flavonoids, fatty acids, polysaccharides
- Documented antiandrogenic, antiestrogenic, antiinflammatory effects
- Used in treating photoaging

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**Saw Palmetto Mechanisms of Action**

- Antiestrogenic
- Antiandrogenic
- Anti-inflammatory
- Antimicrobial
- Anti-proliferative
- Cyclo- and lipo-oxygenase inhibitor
- COX-2 inhibitor

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**Saw Palmetto Active Secondary Metabolites**

- Sterol
- Flavenoid
- Free fatty acids
- Polysaccharides
Ginseng

- Panax quinquefolius
- Enhances immunity, protein synthesis, and tumor toxicity

Ginseng Mechanisms of Action

- Treats extrinsic aging
- Anti-inflammatory
- Antioxidant
- Antitumor
- Treats hyperpigmentation
- Treats atopic dermatitis
- Antipruritic
- Stimulates hair growth
- Inhibits prostaglandin synthesis
- COX-2 inhibitor

St. John’s Wort

- Hypericum perforatum
- Wound healing effectiveness via antistaphylococcal, anti-inflammatory activity, T lymphocyte stimulation
**St. John’s Wort**

- Source of essential oils, glycosides, hypericin, pseudohypericin, resins, rutin, tannins
- Used topically to treat abrasions, bruises, muscle aches and inflammation, minor burns, neuralgia, insect bites and stings
- Functions: anti-inflammatory, antioxidant, astringent

**St. John’s Wort Clinical Studies**

- 21 patients, blinded clinical trial with 1.5% hypericum cream showed improvements in mild to moderate atopic dermatitis

*Draelos ZD, Thaman LA. Cosmetic Formulation of Skin Care Products, Taylor and Francis, New York 2006;329.

**White, Black, Oolong Tea**

- Camellia sinensis
- Inhibits cutaneous photodamage, carcinogenesis, and inflammation
- Can be used to alleviate hypersensitivity reaction and atopic dermatitis
**White, Black, Oolong Tea**

- All shown to display anti-inflammatory (via cyclo-oxygenase II inhibition), antioxidant, antitumor, and chemoprotective effects as well as inhibit angiogenesis, UVB-induced erythema and DNA damage while improving DNA repair and immunity.

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**Tea Tree Oil**

- Derived from essential oil of Melaleuca alternifolia
- Tea tree oil effectively treats acne, onychomycosis
- Possesses antimicrobial properties


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**Tea Tree Oil**

**Mechanisms of Action**

- Antihistamine
- Anti-inflammatory
- Antimicrobial
- Treats rosacea
- Treats tinea
- Teats acne
- Estrogenic
- Drug delivery
**Tea Tree Oil Clinical Studies**

- Double-blind controlled clinical trials have shown 5% tea tree oil gel equally effective as benzoyl peroxide in treating acne but with less irritation.

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**Chamomile**

- Matricaria recutita
- Active secondary metabolites
  - Flavonoids
  - Quercetin
  - Bisabolol
  - Terpenoids

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**Chamomile Clinical Studies**

- Topical chamomile cream superior to 0.5% hydrocortisone for treating dermatitis and sunburn
- Statistically significantly decreased wound area and healing time

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**Lavender**

- Lavandula angustifolia
- Anti-inflammatory and antimicrobial activity
- Inhibits mast cells
- Therapeutic for wound healing, acne, herpes, psoriasis

**Lavender Active Secondary Metabolites**

- Flavonoids
- Triterpenes
- Tannins
- Coumarins

**Lavender**

- Functions
  - Antihistamine, antimicrobial, analgesic, antitumor, estrogenic
- Cytotoxic to fibroblasts if lavender concentration exceeds 0.25%
Linden Extract (Tilia)

- Bark extract from Linden tree
- Antispetic, skin-clearing, soothing, sedative, circulation-stimulating, hydrating, and astringent properties
- Used to help irritated or troubled skin

Lentinula Edodes (Shiitake Mushroom Extract)

- Contain polysaccharides, triterpenes, proteins, lipids, phenols, and cerebrosides

Shiitake Mushroom Extract

- Shown to possess potent antioxidant and anti-inflammatory properties
  - Inhibition of lipid peroxidation, superoxide dismutase, metalloproteinases, and proinflammatory cytokines
  - Promotion of free radical scavenging
  - Inhibits elastase (breaks down elastin) and activator protein-1 (breaks down collagen)
  - Stimulates growth of epidermal cells
**Mushroom Extract Clinical Study**

- Effectiveness of mushroom complex serum to improve appearance of photoaged facial skin evaluated in 31 women with moderate photodamage
- Significant improvements in skin texture, clarity, overall photoaging, fine lines, and pigmentation within 8 weeks


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**Cucumber Extract (Cucumis Sativus)**

- Moisture-binding, moisture-regulating, soothing, tightening, anti-itching, refreshing, softening, healing, and anti-inflammatory properties
- Contains amino acids and organic acids that strengthen skin’s acid mantle
- Effective in eye treatment products, tightening agent, and for oily skin

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**Spirulina Extract**

- Hydrating effect on skin’s surface layers
- Certain spirulina proteins contribute to stimulation of fibroblast and to tissue regeneration

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Eyebright Extract (Euprasia officinalis)
- Herb credited with astringent, anti-inflammatory, and tonic properties
- Used in eye care products to decrease and counteract eye area inflammation and potential irritations
- Important constituents include tannin, mineral salts, iridic glycosides

Willow Bark Extract (Salix)
- Antiseptic and skin clearing properties
- Roots and leaves have demulcent, tonic, and astringent properties

Arnica Montana
- Antiseptic, astringent, antimicrobial, antiallergenic, anti-inflammatory, anticoagulant, circulation-stimulating, healing, and stimulating properties
**Arnica Montana**

- Promotes removal of wastes from skin, aids in promotion of new tissue growth
- Effective in gels and creams designed to treat damaged, reddened, or tired skin
- Important constituents: arnicin, tannin, phulin, sesquiterpenes, flavonoids, and coumarins