Professional Disclaimer

• Dr. Richard Brown and Dr. Patricia Gerbarg have no conflicts of interest regarding this lecture.

• The do not receive any financial benefits from the promotion or sale of the supplements mentioned in this lecture.

• They are co-authors on some of the references included in this lecture.
Consultation with your doctor is advised before trying supplements for serious illnesses such as COVID-19.

- Some of the treatments covered in this lecture have been tested for efficacy against COVID-19 in vitro or in vivo.
- Some treatments have been tested against infections that have similar properties, e.g. other coronaviruses, influenza, respiratory infections, or inflammatory conditions.
- Some of the treatments which we have found to be beneficial in patients treated in clinical practice, have not yet been tested in controlled studies of COVID-19, but are promising candidates for further study. These are low in side effects and could be tried to improve immune defense or recovery from COVID-19.
Treatment Targets for Coronavirus

• Anti-viral: cell penetration, replication of viral RNA
• Anti-inflammatory: dysregulated cytokine and immune response “cytokine storm”
• Anti-stress: anxiety, depression, PTSD

Recovery from COVID-19

• Post-infection symptoms can last for days or months:
  • chronic fatigue, myalgia (muscle aches)
  • Anxiety, depression, PTSD
  • cognitive dysfunction
  • persistent respiratory symptoms

Post-COVID Fatigue

• 30 - 50 % hospital discharged COVID patients
• Chronic Fatigue Syndrome needs further study in this population
• Findings of autonomic nervous system exhaustion underlying Chronic Fatigue, PTSD, Fibromyalgia Syndrome are similar.
• In US most common events preceding CFS have been car accident or severe infection (e.g. influenza, Lyme disease)
• After other symptoms resolve, patients report extreme fatigue, frequent long naps, erratic sleep cycles

Herbs and Nutrients

• Adaptogens: Rhodiola rosea, Eleutherococcus senticosus, Schizandra chinensis
• Red Mangrove of Fiji (Rhizophora mangle)
• Black elderberry (Sambucus nigra)
• Beta Glucan from mushrooms
• Olive Leaf Extract (Olea europaea)
• Green chiretta (Andrographus peniculata)
• French Oak wood Extract (Quercus Robur Extract)
• Zinc
• Traditional Chinese Medicine (TCM)
Adaptogens

• Arctic root, Golden root (Rhodiola rosea)
• Chinese magnolia, Schizandra (Schizandra chinensis)
• Siberian Ginseng (Acanthopanax or Eleutherococcus senticosus)
• Asian Ginseng (Panax ginseng)
• Ashwaganda (Withania somnifera)
Defining Adaptogens

• Herbal extracts Protect against multiple stressors
• increase attention and endurance under stress
• reduce/mitigate/prevent stress-induced impairments and disorders related neuro-endocrine-immune systems.

• **Metabolic Regulators**
  • Cellular repair: mitochondria, heat shock proteins, neuropeptide Y, glucocorticoid receptors
  • Roots contain many Antioxidants
  • Epigenetic effects

  (A Panossian & G Wikman, 2009)
Single Dose Adaptogen Effects

• R. rosea, S. chinesis, E. senticosus
• SAS stimulation
• No addiction, tolerance, abuse, rebound hypersomnolence
• R. rosea most active stimulating effect in 30 min lasts 4-6 hrs
• HPA axis adaptation to repeated stress by multiple doses

Molecular Mechanisms of Adaptogen Rhodiola rosea (Arctic root)

- **Metabolic Regulators**
- Rich in antioxidants
- Increase ATP (energy transport molecules) and Creatine in brain cells
- Enhance Cellular repair: mitochondria, heat shock proteins, neuropeptide Y, glucocorticoid receptors
- Epigenetic effects

**Rhodiola rosea** (Artic Root, Roseroot)

- Adaptogen: improve energy, mood, focus, memory
- Enhance physical and mental performance under stress
- Stimulative effects can be additive
  - Caffeine in coffee, sports drinks
  - Mild anti-platelet at higher doses (above 800 mg/day)
- Patients susceptible to stimulative effects
  - Anxiety disorder, Bipolar disorder, Elderly
  - Patients with underlying cardiac arrhythmia

**Rhodiola rosea**

- Dose bell curve: 50–800 mg/d; average 300-450 mg/d
- 95% ethanol R. rosea root extracts (Norway) showed *in vitro* inhibition of CYP3A4 and P-glycoprotein (P-gp).
- SHR-5 extract fed to rats with two CYP450 substrates, warfarin and theophylline. *R. rosea SHR-5* *in vivo* had no significant effect on CYP450, theophylline pharmacokinetics, or warfarin pharmacokinetics or anticoagulant activity.
- No published *in vivo* studies of *R. rosea* effects on P-gp or serum levels of digoxin

SHR-5 Rhodiola rosea for Depression

- RDBPC 6-wk trial mild-mod depression
- N = 60
- A - 340mg/d  B – 680mg/d  C – placebo

Mean drop in Scores

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↑self-esteem

Clinical Uses for Rhodiola rosea

• Relieve fatigue and cognitive dysfunction caused by medical illness or medications
• Anti-bacterial and anti-viral (Coxsackievirus B3, Hepatitis C)
• Increase energy, motivation
• Improve mental and physical and endurance
• Antidepressant
• Improve age-related decline in memory and cognitive function

Additional Benefits of Rhodiola rosea

• Improve stress tolerance and resiliency for physical and emotional stress
• Prevent/Treat Post-traumatic Stress Disorder
• ADHD – helps improve mental focus
• Improve cognitive recovery from neuro-lyme disease
• Prevent/relieve: high altitude sickness, jet lag
• Used for sexual enhancement
• Antibacterial
ADAPT: Rhodiola rosea, Eleutherococcus senticosus, Schizandra chinensis

• Improved ANS balance, function and resilience
• Corrects abnormal levels of neuropeptide Y (also found in PTSD)
• Suggested Treatment:
  a. R. rosea (Rosavin by Ameriden or Energy Kare by Karenherbs.com)
  b. E. senticosus + S. chinensis (Kare-N-Liver by Karenherbs.com)

Rhodiola Side Effects

- Excess stimulation
- Bipolar – caution, may induce mania
- Vivid dreams (usually not nightmares)
- Rare sedation
- Rare hypersexuality
- Rare agitation with ↑ BP in post MI patients
- Mild GI upset
- Advise not to combine with MAOIs
Administration of *Rhodiola Rosea*

- 20 minutes before food (breakfast and lunch) or 2 hours after a meal
- Start 1 capsule AM (100-150-170-180 mg)
- Increase by 1 cap/tab every 3-14 days
- Average dose 300-600 mg/day
- High dose: 900 mg/day
- Above 900 mg risk of bruising increases
Quality Rhodiola Rosea Brands

• **Energy-Kare**: Kare-n-Herbs 180 mg tab (4% rosavins) (higher potency)

• **Rosavin**: Ameriden 100 or 150 mg (3% rosavins)

• **Arctic Root**: Swedish Herbal Institute 180 mg (4% rosavins)
ADAPT Formula

• Balance of adaptogens to optimize physical and intellectual performance under stress: mental alertness with emotional calmness
  • Rhodiola rosea
  • Eleutherococcus senticosus
  • Schizandra chinensis

(Brown RP, Gerbarg PL. How to use Herbs, Nutrients and Yoga in Mental Health; The Rhodioal Revolution)
Eleutherococcus senticosus
(Acanthopanax or Siberian ginseng)

*In vitro* & animal studies: inhibits P450 enzymes 1A2, 2C9, 2D6, and 3A4.

Human studies: no impact on CYP3A4 or CYP2D6, no clinically significant change in isozymes. No effect on digoxin.

(Kennedy & Seely, 2010)
Schisandra chinensis

*In vitro:* inhibits CYP3A4 enzymes.

*In vivo:* induces CYP3A4

Animals: decreased warfarin levels

Humans: no change in warfarin levels

ADAPT for Cognitive Performance

• ADAPT-232: Rhodiola rosea + Eleutherococcus senticosus + Schizandra chinensis
• DPRPC 40 women (20-68 yo) c/o chronic stress
• 1 dose ADAPT or placebo → 2 hrs later stressful cognitive tests
• ADAPT significantly improved focus, processing speed, and accuracy.

Red Mangrove Tree of Fiji - Rhizophora mangle

- Long use for activating protective cells in respiratory tract
- Numerous antiviral, immune enhancing, anti-inflammatory, antinociceptive constituents:
  - Flavonols (Kaemferol, quercetin)
  - 7-hydroxycoumarin (does not affect coagulation)
  - Polyphenols
  - Glucans
  - Hexose
- Quercetin Suppresses proinflammatory cytokine production in macrophages. Could reduce “cytokine storm”

Red Mangrove Tree of Fiji - Respigard®

• Directions on bottle.
• Limited supplies
• Nature’s nurse uses sustainable harvesting techniques, but new groves of trees are much needed.
Black Elderberry Syrup from European elder (Sambucus nigra)

- Inhibits viral replication
- Long traditional use for flu, respiratory infections
- Controlled studies are needed.

- Nature’s Way Sambucus
- No need to get formulas with added ingredients
- Acute infection: 2 tsp 4x/day
- Prevention: 1 – 2 tsp/day
Rhodiola rosea root, Sambucus nigra fruit, and Nigella sativa seeds

- Infectious bronchitis virus (IBV) a chicken coronavirus
- Vero cells pretreated with extract, infected with virus, incubated
- Herbal extract inhibited viral replication

(Chen C. BMC Vet Res. 2014.10:24)
373 extracts from 128 TCMs tested for Anti-Ebola Virus Effects

- Rhodiola rosea: potent inhibition of cell entry for Ebola and Marburg
- Polyphenols Ellagic Acid and Gallic Acid: most effective constituents
- French Oakwood Extracts also contains ellago-tannins (ellagic acid + tannins)
- Rhodiola enhances cellular immunity and humoral immune function in animal model
- Rhodiola inhibits Dengue Virus multiplication.
- Salidroside boosts host immunity and inhibits viral protein synthesis

Beta Glucan

• Extract from cell walls of mushrooms, yeast
• Immunomodulatory and cytoprotective
• Beta Factor from Ameriden.com
• 1 – 2 caps/day taken on empty stomach
Shiitake mushroom (*Lentinus edodes*)

- β-glucan extracts reduce pro-inflammatory cytokines and oxidative stress.
- Immunomodulatory and cytoprotective properties in ‘house’ (IH-Lentinan, IHL) and commercial (Carbosynth-Lentinan, CL) extract in vitro models of lung injury and macrophage phagocytosis.
- CL higher amounts of α-glucans; less β-glucans. Both extracts reduced cytokine-induced NF-κB activation in human alveolar epithelial A549 cells. In activated THP-1 derived macrophages, CL more effectively attenuated pro-inflammatory cytokine production (TNF-α, IL-8, IL-2, IL-6, IL-22) and TGF-β and IL-10. CL extract attenuated oxidative stress-induced early apoptosis; IHL extract attenuated late apoptosis.
Olive Leaf Extract

• salidroside (tyrosol), adaptogen used to protect against many infections for several hundred years
• polyphenols, notably oleuropein and hydroxytyrosol, that have antiviral, antibacterial, anti-inflammatory and antioxidant properties that may reduce Upper Respiratory Infections
• Evidence of inhibiting viral replications in vitro
• Olive Factor from Ameriden - 2pills 2x/day

(Somerville V, The Effect of Olive Leaf Extract on Upper Respiratory Illness in High School Athletes: RCT. Nutrients. 2019; 11(2): 358.)
Creat or Green Chireta (Andrographis peniculata)

- Protects against influenza.
- Native to India and Sri Lanka
- No data for COVID-19 yet.
- Kold Kare from KarenHerbs
- 1 pill 1-2 X/day for prevention
- 1 pill 4x/day when symptoms
Zinc

• Essential for immune function
• Considerable data on zinc inhibiting viral replication
• 25% of population in developing countries have zinc deficiency
• Zinc deficiency associated with compromised immune defense
• In China: 100 – 200 mg/day are used, but these doses can cause toxicity and block copper absorption
• Safety for various lengths of use is unknown

(Read SA et al. Role of Zinc in anti-viral immunity. 2019 Jul 1;10(4):696-710.)
French Oak Wood Extract (Robuvit)

• RCTS showed benefits for CFS and PTSD
• Helpful for CFS
• Reduced oxygen free radicals and homocysteine
• Contains 40% polyphenols called ellagotannins. Also found in Red Mangrove tree of Fiji
• 20 cases relieved fatigue after COVID-19 [Dr. Brown’s practice]
French Oak Wood Extract References


Traditional Chinese Medicine (TCM)

• Role of TCM herbs is unclear and requires training in Chinese Medicine, acute observation of the patient, takes time to obtain

• Low quality of research published – controlled studies needed

• Screening hundreds of herbal formulas now to identify most promising compounds for in vitro and in vivo testing

Current and Future Directions: Prevention & Recovery

• Determine natural compounds that can have anti-viral effects and which can prevent humans from infection by this coronavirus
  • Molecular docking to find high binding affinity between the herbal compound molecules and the COVID-19 receptor
  • Prevent entry into human cells
  • Prevent replication of virus RNA and/or damage viral cells

• Identify natural compounds with known anti-inflammatory effects for trials in COVID treatments

• Synthesize molecules and evaluate in vitro, in animal models and in humans for activity against COVID-19

• Trials of natural compounds known to reduce symptoms similar to those in post-COVID patients: fatigue, myalgia, depression, PTSD, cognitive dysfunction, pulmonary fibrosis
Integrative Psychiatry Resources

• *How to use Herbs, Nutrients and Yoga in Mental Health Care*

• *Complementary and Integrative Treatments in Psychiatric Practice*
  Ed. Gerbarg PL, Brown RP and Muskin PR.
  American Psychiatric Association Publishing, 2017

• **www.Breath-Body-Mind.com**
  RP Brown & PL Gerbarg. Updates Integrative Psychiatry, Videos, Workshops

• **American Psychiatric Association CAIM Caucus:**
  [https://www.psychiatry.org/psychiatrists/practice/professional-interests/integrative-medicine](https://www.psychiatry.org/psychiatrists/practice/professional-interests/integrative-medicine)
Online Resources Websites

Breath Pacing Audio Track: https://naturalsinger.com/5-breaths
Breath-Pacing 2-Bells track (60 Minutes): Spotify [App], Amazon.com, Coherentbreathing.com

www.RobertPeng.com QiGong DVDs, meditation CDs

www.STWS.org – low fee and pro bono BBM programs for disaster survivors, first responders, veterans

www.globalgrassroots.org (women’s empowerment) programs in Africa

www.nolimitgen.org (child refugees) Free Child teaching Videos

HealthFlix.online (youtube)Webinars with Dr. Brown & Dr. Gerbarg
Key References


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• Alexander Panossian. Adaptogens in Mental and Behavioural Disorders. Psych Clin NA. March 2013, 36(1):


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Recommended Reading


©PLGerbarg & RPBrown 2016


• Gerbarg PL, Jacob VE, Stevens L ... Brown RP, Scherl EJ. The Effect of Breathing, Movement, and Meditation on Psychological and Physical Symptoms and Inflammatory Biomarkers in Inflammatory Bowel Disease: A Randomized Controlled Trial. J Inflammatory Bowel Disease. 2015 Dec; 21(12):2886-96.


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