Mentoring the Mentor

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Eternal Truth

He who does not use his endeavors to heal himself is brother to him who commits suicide.

Proverbs 18:96

Mentor goals:
- To declare what is possible and establish a commitment to that possibility
- Address personal and professional barriers limiting the ability to serve
- Evolution of vision/mission/ethics that drive success
- Create immediate action steps to apply learning and growth
- Construct the round table of applied trophologists
Mentoring the mentor:

- Who are the mentors? – Practitioners
- Who are we mentoring? – Patients and GAP
- What’s the purpose? – Optimized life
  - How does it work? – Whatever you learn you teach someone else (anyone else)
- Who’s is included? – Self selection, you pick yourself

Mentoring the mentor:

- Each participant attends monthly teleconferences (1 hour in duration, 4th Wednesday of every 2nd month) creating a round table discussion/exploration of the dynamics and details of a nutrition-based holistic practice
- Each participant chooses how to convey the notes and information to their world and community – no information squandering

Review - Distinguish yourself

- It is more apparent why people are choosing alternative health care professionals who specialize in a functional approach
- No matter you specialty or technique you must distinguish yourself as an expert – people are just seeking to understand and they need you to do so
- Typically in the healthcare industry people are receiving shallow answers that leave them puzzled with the mystery of “Why is this happening to me?” and “What can I do about it?”
- Trends research over 10 years ago identified a number of factors essential to being successful in the nutritional field – one of those was establishing yourself as an expert
According to your DNA, from all recorded learning and adaptation, the number one cause of death is infection.

All effort shall be to survive that.

Research + Experience

You Will

Hypothesis -

The only reason why anything that ever was working, stops working is because of infection
Science

Science is the description of the mechanized nature of reality. Why and how it works, and how to make it work – every time. As it studies the details of how things work it knows, all the rest it just hasn't discovered yet …

Our practices are pure science – because they describe and document what works or not, and they never stop discovering new things … So we can make things work at will …

Immune System – Mammalian

Immune development increased survivability of organisms which promoted more sophisticated species evolution.

It permitted clarified DNA purity which increasingly ‘got the message out.’ Before immune development lifespans were brief and primarily unicellular.

Immune – ‘Immun’ means free

“If you’re not with us, then you’re against us”

It was always a competition for control of the creative DNA and the cellular machinery to support life

IDRS – Immune Defense Repair System

Functional term which includes the idea that the enabled immune system in addition to defending also repairs cellular structure and promotes DNA to proteomics to metabolomics translation accuracy

Immunity creates autonomy and selfhood
Immune Organization -

**Innate Immunity (Non-specific):**
A lowly foot soldier responding within minutes to all foreign invaders.

**Barricades (2 lines of defense):**
2. Inflammation mitigated through antimicrobial proteins, phagocytes and cells to inhibit movement through the body.

**Adaptive Immunity (Specific):**
Infiltrating Barricade (3rd line of defense):
Requiring more time to mount this system was first revealed in the late 1800’s showing animals developed antibodies.

- **Antigen Specific** – recognizing antigens
- **Systemic** – not restricted to initial infection site
- **Memory** – after initial exposure more severe defenses are mounted

**Innate & Acquired Immunity**

Primary roles of the healthy immune system are:
- Identify potentially injurious and infectious substances
- Distinguish self antigens (non-threatening) from non-self (threatening)
- Assess the potential level of threat posed by infectious, toxic, or non-self antigens
- Mount a response that is appropriate to the level of threat
- Repair any damage that ensues from adversarial encounters

**Too much response = inflammatory cascades**
**Too little response = tolerance of danger**

WBC is optimal 6-8, outside optimal range may suggest acute or chronic immune burden, under 4 indicates bone marrow fatigue

**Immune System – 2 Parts**

Generally recognized that there are 2 parts of the immune system

**Innate Immune System** – Inborn initial response to eliminate microbes and infections immediately or within hours — it is not in any locale or organ, it is in the WBC.

- Each cell is equipped with different mechanisms that allow it to attack and eliminate pathogens from the body demonstrating immune versatility
- Non-specific defense against pathogens, activates the complement system of inflammatory response
- Identifies self vs. non-self, complement system triggers inflammation and identifies foreign substances, and activates the adaptive immune system

**Innate Immune Cells include:**
- Mast Cells
- Natural Killer Cells
- Phagocytes – Monocytes, Macrophages, Dendritic cells
- Neutrophils – Neutrophils, Eosinophils, Basophils

**Adaptive Acquired Immune System** – Learned response precisely addressing threat requiring 5-7 days for adaptive immune modulation to reach full activity and specific lymphocyte presence

- Results in TH1 cellular phagocytosis or TH2 humoral antibodies
- TH1 responds to living things (bacteria, fungus, virus)
- TH2 responds to non-living things (and parasites) including food, pollen, bad fats, heavy metals.
**Immune Structure**

![Immune System Diagram]

**Innate Immunity**

Surface Barriers – skin (keratinized) and mucosae line all exterior surfaces (Skin, Digestive, Respiratory, Urinary, Reproductive)
- Acidity of skin/vagina is pH 3 to 5
- Stomach Acid
- Lysozymes in saliva and lacrimal fluid
- Sticky mucus traps/antiseptic paint
- Ciliated surfaces

Body has many nonspecific cellular and chemical devices for protection.
- Phagocytes
- Natural killer cells
- Antimicrobial proteins
- Inflammation targets immune system for defense and repair
- Fever

Barriers are effective but when breached internal innate immune defenses come into play.

**Innate Immunity**

Innate immunity is responsible for the immediate response to a pathogen - within hours

During the initial stages of a viral infection the cytokines generated by the innate immune response account for most of the symptoms experienced

Antimicrobial peptides such as **defensins** are also released, interferons, iron-binding proteins

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**Innate Immunity**

Key cells of innate immunity

**Phagocytes:**
- Monocytes (in the tissue become macrophages)
- Macrophages (The big eaters – wandering/free and fixed Kupffer Cells in the liver and microglial brain) – in search of cellular debris or invaders
- Neutrophils (most abundant WBC)
- Eosinophils (position against Helminth and discharge destructive cytoplasmic granules over the invader)
- Basophil (Anti-parasitic)
- Mast cells (weakly phagocytic to wide range of invaders)


**Cytokines – Immune Messages**

Immune response results in the release of cytokines meant to direct local and distant immune function

These cytokine messenger molecules also drive HPA status and thus determine global brain status

Cytokines subsequently cause the release of WBC inflammatory mediators to direct the inflammatory process of repair

Therefore immune status and activity determine HPA/brain settings

Hypervigilant or depressed immune states reflect in brain states
Cytokines – Immune Messages

The HPA Axis is the conductor of homeostatic symphony. This system additionally intertwines with virtually every aspect of physiology through the production of CRH and ACTH—indeed resistant and “hard-to-treat” conditions all share the described cytokine cascade disturbance. The take away is that any chronic perturbation to one element of the system will ripple through other components of the web. Persistent stressors without relief continuously stimulate the CRH-ACTH-cortisol axis resulting in high levels of cortisol and some neuronal disruption and death in the negative feedback loop (hippocampus and hypothalamus). This may lead to depression and behavioral disturbance.

Cytokines – Immune Messages

So the immune modulation and unburdening is required to achieve HPA and endocrine balance. The concept of immune sparing and unburdening is essential to any long term concept of HPA integrity. The sequential immune up-regulation is the avenue to HPA strength and health. The HPA axis will not completely balance and limbic health will not be achieved without immune and cytokine support.


Cytokines signal in the brain: Saturable transporters, BBB leakiness, localized production, binding to receptors on afferent nerve fibers, recruitment of activated cells.
The human body does not have a single immune organ, however it is in itself an immune system comprised of:

- **Thymus** (where the immune cell matures)
- **Long bones - Marrow** (where the lymphocyte originates)
- **Spleen** (activity of the leucocytes)
- **Liver** (activity of inflammation and autoimmune response)
- **Stomach** (HCL is needed to destroy ingested bacteria, virus, and parasites)
- **Intestinal flora** (destroys pathogenic microbes, stimulates interferon production)

*It has been said that 90% of our immune system is in our gut!*
There are three primary systems that influence the immune virulence:

1. Neuro-Endocrine
2. Hepatic / Splenic
3. GI / Gut Biome

Talking together through Cytokines
**Pattern Recognition Receptors (PRRs)**

- PRRs are involved in innate immune recognition and responses.
- PRRs recognize components of micro-organisms that are not found on the host → PAMPs (pathogen-associated molecular patterns)
- PRRs are found on the cell membrane and also within the cell
- Toll-like receptors (TLRs) are the most common class of PRRs and each recognizes a distinct bacterial, fungal or viral molecular pattern

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**PRR**

Activation of the Toll-like receptors communicates the outside to the cytoplasm and then through the nuclear membrane in a similar fashion to the inner DNA.

These are like transformer step down conveyances of the outer world to the inner.

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Figure A: Basic Signaling of Pattern Recognition Receptors. See text for explanation.
MHC Proteins – Self

Major Histocompatibility Complex (MHC)

The external surface of cells is dotted with a variety of protein molecules, of which some are individually unique glycoproteins that mark the cell as 'self'.

Every genetic expression of proteomics carries these 'self' MHC markers.

Class I MHC proteins are found on all cells of the body.

Class II MHC proteins are displayed only by certain immune-acting cells.

Each MHC molecule has a deep groove which displays peptides from the breakdown of cellular proteins.

Infected cells have fragments of foreign antigens bound to the MHC resulting in immune activation.

Common TH1 & Th2 Cytokines

TH1
- IL-12
- IFN-γ
- TNF-α
- IL-2
- GM-CSF

TH2
- IL-4
- IL-5
- IL-10
- IL-13

IL-1 and IL-6 (and others) can show both TH1 and TH2 influences

PRR’s and Inflammation

Immune signaling is primarily activated through a host of receptors called pattern recognition receptors (PRR)

The first PRR discovered was the Toll-like receptor found in 1998 – since then there have been ten Toll-like receptors discovered.

C-type lectin receptors (CLR) are similar detecting helminths, fungi, mycobacterium – Dectin-1 is a CLR that responds to pathogenic and immunomodulating fungi

Retinoic acid-inducible gene 1 (RIG-I) recognizes viral RNA and signals viral response

Nucleotide-binding and oligomerization domain (NOD) can see PAMP and DAMP and regulate inflammatory response

When one or more PRRs recognize an antigen a cascade of intracellular signaling results in cytokine upregulation of the Nrf4B inflammatory mechanism

PRR recognition directs the naïve Th0 maturation

A class of NOD-like receptors (NLR) produce complexes called inflammasomes
Typical inflammasome is comprised of 7 molecules which facilitate pyroptosis and programmed cell death.

It is currently known to be triggered by LDL particles, high glucose, cholesterol crystals and certain fatty acids – this is the critical modulator of low-level inflammation of cardiac disease.

Bioactive plant compounds EGCG, luteolin, quercetin, chrysin have been shown to inhibit downstream signaling by PRR activation thus dampening inflammatory amplification.

Curcumin and Feverfew have been shown to inhibit signaling from NLR.

Prepare for a new class of herbal and nutrient tools driven by the now visible mechanisms and the confidence to support them.
Modulating PRRs

A key to supporting immune function is modulation of the PRR.

PRR activation requires dimer formation (homodimers and heterodimers).

A number of phytochemicals have already been shown to affect PRR function and signaling.

Recent studies show curcumin, sulforaphane and cinnamaldehyde are able to reduce PRR dimerization and reduce TLR signaling.

Anything’s possible …

Virgil

77 years old, surgical recommendation of left leg amputation due to hospital acquired MRSA Staph infection– attempted supplementation resulted in onset of 3 boils 2 days later ultimately porting and total amelioration of infection.

Daniel

Chronic abscess under left lower molar with recommendation for extraction prevented through porting and remarkable gum recovery.
Chin Lao – 67 years old entered hospital for routine angioplasty procedure for cardiac ablation to correct arrhythmia – hospital acquired infection in the groin resulting in 60 days in hospital, five rounds of IV antibiotics, Sartorius muscle graft and complete removal of all lymph structures in the groin, sent home to die. Entered with severe weakness, entire leg swollen and febrile – 1 month later walked in with 95% of heat in leg gone, graft repairing – the game is on!

**Immunosenescence**

Immune aging – described as a loss of immune reserve and a loss of immune discretion at the same time.

Some immune features decline while others increase (antibody production and inflammatory upregulation).

These changes increase susceptibility to infectious disease, poor immunization response, cancers, autoimmune dysregulation.

Increased inflammation is called ‘inflamaging’.

**Factors determining rate of immune decline:**

- High cortisol to DHEA ratio
- HGH reduction
- Thyroid decline
- Antioxidant depletion
- Immune burdening
- Stress
- Sleep loss of quality/quantity
- Diet (Elevated HgA1C)
- Exercise reduction
**Molecular Basis of the Aging Process in the Immune System**

**Altered Transcription Factors**
- Reduced gene expression
- Increased gene expression

**Inflamed Age**
- Inflammatory cytokines
- Increased cell death

**Increased Immune Regulation**
- Reduced immune response
- Increased immune response

**Immune Senescence**
- Decreased immune function
- Increased immune dysfunction


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**Factors Affecting Aging**

- Decreased immune function
- Increased immune dysfunction

- Decreased gene expression
- Increased gene expression

- Genome Instability

- Oxidative Stress

- DNA Damage Repair

- Mitochondrial Function

- Age-Related Changes Impacting Immune Function

Figure 8: Age-Related Factors Affecting Immune Function. Adapted from: Liewolf SL, Gao Y. (2015). 1031-1041.

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**Guide to Longlife**

**The Prevention of Inversion Hierarchy**

<table>
<thead>
<tr>
<th>Maintenance &amp; Repair</th>
<th>Augmentation</th>
<th>Acceleration</th>
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<tbody>
<tr>
<td>Inflammation &amp; Stress</td>
<td>Repair &amp; Recovery</td>
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Dr. Stuart White  Mentoring the Mentors  5/16/2018
Aging and thinking ...

When you are 18 years old you worry about what others are thinking about you.

When you are 40 you don’t care what others are thinking about you.

When you are 60 you realize that no one is thinking about you at all

Candida Questionnaire -

Candida Purification 90 Day Diet
Immune Modulation
An Immune Paradigm

Gut Flora Complex

- Anise (Pimpinella anisum) fruit essential oil 125 mg
- Andrographis paniculata aerial parts 10:1 extract from Andrographis paniculata aerial parts 1.0 g 100 mg
  Containing andrographolide 10 mg
- Phellodendron amurense stem bark 20:1 extract from Phellodendron amurense stem bark 1.6 g 80 mg
  Containing berberine 36 mg
- Oregano (Origanum vulgare) leaf essential oil 75 mg

Cataplex® AC

- Vitamin A 1,500 IU
- Vitamin C 11 mg
- Proprietary Blend: 490 mg Echinacea (root)*, calcium lactate, sweet potato*, carrot (root)*, bovine adrenal*, bovine kidney*, nutritional yeast*, magnesium citrate, alfalfa flour*, dried alfalfa (whole plant) juice*, mushroom*, dried buckwheat (leaf) juice*, buckwheat (seed)*, bovine bone*, defatted wheat (germ)*, oat flour*, sunflower lecithin*,veal bone*, vitamin E (sunflower), rice bran*, and carrot oil*
### Black Walnut Hulls

- **Black Walnut Hull 1:10 extract**
  - *Juglans nigra* hull 500 mg
  - 5 mL

### Echinacea Premium

- **Calcium**
  - 90 mg

- **Echinacea root 4:1 extract**
  - *Echinacea angustifolia* root 600 mg
  - Containing alkylamides 2.0 mg
  - 150 mg

- **Echinacea root 6:1 extract**
  - *Echinacea purpurea* root 675 mg
  - Containing alkylamides 2.1 mg
  - 112.5 mg

### Andrographis

- **Calcium**
  - 40 mg

- **Echinacea root 4:1 extract**
  - *Echinacea angustifolia* root 500 mg
  - 125 mg

- **Holy Basil herb 5:1 extract**
  - *Ocimum tenuiflorum* herb 500 mg
  - 100 mg

- **Andrographis herb 10:1 extract**
  - *Andrographis paniculata* herb 1.0 g
  - Containing andrographolide 10 mg
  - 100 mg

- **Holy Basil (*Ocimum tenuiflorum*) herb essential oil**
  - 10 mg
  - 57 mg
Artemisinin

- support normal flushing of natural toxins from the body
- encourage healthy function of organs of elimination
- cleanse the blood
- encourage healthy bowel function
- support healthy digestion
- support a healthy intestinal environment*

Myrrh

- support healthy bowel function
- support healthy digestion
- support a healthy intestinal environment
- support gastrointestinal health
- support sinus and respiratory health*

Wormwood Complex

<table>
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<th>Ingredient</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Calcium</td>
<td>20 mg</td>
</tr>
<tr>
<td>Stemonan root 5:1 extract from <em>Stemonan sessilifolia</em> root</td>
<td>200 mg</td>
</tr>
<tr>
<td>Black Walnut hull 4:1 extract from <em>Juglans nigra</em> hull</td>
<td>25 mg</td>
</tr>
<tr>
<td>Wormwood herb 4:1 extract from <em>Artemisia absinthium</em> herb</td>
<td>25 mg</td>
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</table>
The Ganoderma and Shiitake mushrooms contain several types of polysaccharides, triterpenes, amino acids and other compounds. The combination of these unique mushrooms can help to:

- Promote the body's normal resistance function
- Promote vitality
- Stimulate healthy immune system response
- Encourage adaptive response to occasional everyday stress*

Thymex

- Cholesterol: 5 mg
- Vitamin C: 5 mg

Proprietary Blend: 370 mg
- Calcium lactate, bovine thymus Cytosol™ extract†, and magnesium citrate.
Sesame Seed Oil

Sesame Seed Oil contains essential fatty acids, as well as naturally occurring vitamin E. Provides antioxidants. Supports healthy liver function. Supports immune system function.

Livco

- Calcium: 90 mg
- Schisandra fruit 6:1 extract from Schisandra chinensis fruit: 1.0 g
  - 167 mg
- Rosemary leaf 5:1 extract from Rosmarinus officinalis leaf: 500 mg
  - 100 mg
- Milk Thistle seed 70:1 extract from Silybum marianum seed: 2.1 g
  - Containing flavonolignans calc. as silybin: 30 mg
  - 24 mg

Sequential Immune Up-Regulation
Sequential Intervention

- By giving hope through discussion of therapeutic rationale and then accountably determine if the therapy had efficacy it is possible to initiate activity that may assist a person to make the changes that result in healing
- Sequential intervention and accountable follow-up can show what has worked and what may still need to be employed
- Promote an understanding of intervention that creates evolutions in individual physiology and show the effect of that intervention
- Allow every condition to become a strategic consideration of possible etiology and therapeutic rationale – people are in search of experts – reveal yourself
- The comprehensive nature of nutritional therapy means there is always more physiology to optimize and support leaving an individual constantly refining as long as they wish to further improve their status
- If the practitioner is accountable s/he will be allowed to experiment with reasonable ideas

Gut Flora Complex

Anise (Pimpinella anisum) fruit essential oil 125 mg
Andrographis ariel parts 10:1 extract from Andrographis paniculata ariel parts 1.0 g 100 mg
Containing andrographolide 10 mg
Phellodendron stem bark 20:1 extract from Phellodendron amurense stem bark 1.6 g 80 mg
Containing berberine 36 mg
Oregano (Origanum vulgare) leaf essential oil 75 mg

Test for Mold Burden - using Gut Flora Complex

Puncture a perle of GFC and smear on the inside of the wrists and then rub them together
Threaten the mold
Give the body about 2-3 minutes for the mold to perceive the oregano oil and other antifungal compounds and begin to defend itself by releasing mold toxins
Immune reaction occurs
Observe that the ROM and muscular tonicity is reduced and tight with various actions
Limitation proves mold burden
Give orally 1-2 Turmeric Forte and immediately retest the ROM and muscular status
Proves immune modulation
Understanding Chronic Inflammation

Inflammatory Tissue Response

Potential Causes of Chronic Inflammation

- Diet
- Dysbiosis
- Sedentary lifestyle
- Chronic infection
- Stealth pathogens
- Autoimmunity

- Stress
- Oxidative and nitrosative stress
- Obesity
- Fatty liver
- Toxins and drugs
- Trauma
Differential Responses to Increasing Oxidative Stress

**Nrf2**: Master regulator of cellular defenses
**NF-κB**: Master regulator of stress responses, inflammation, cell survival
**AP-1**: Master regulator of cell apoptosis

Importance of Phytochemicals

Turmeric

**Turmeric** (*Curcuma longa*) rhizome has been used widely as a food and traditional medicine. Some traditional uses of the rhizome include:
- Rheumatic pains, traumatic swellings, masses in the abdomen, dysmenorrhea, amenorrhea and for health promotion
- As a blood purifier
- Internally and externally for skin diseases
- Dyspeptic complaints and digestive disorders of hepatic origin
Turmeric Active Constituents

The main constituents of *Curcuma longa* rhizome are yellow pigments, curcuminoids, and an essential oil containing sesquiterpenes.

Curcuminoids comprise:
- Curcumin (60–80%)
- Demethoxycurcumin (15–30%)
- Bisdemethoxycurcumin (2–6%)

“Curcumin” is often used as shorthand for the total curcuminoids.

Curcumin: Key Mechanisms of Action

Nuclear transcription factors:
- Nuclear factor-kB (NF-kB)
- Signal transducer and activator of transcription (STAT) proteins
- Nuclear factor erythroid 2-related factor 2 (Nrf2)

Growth factors:
- Vascular endothelial cell growth factor (VEGF)

Inflammatory cytokines:
- Tumor necrosis factor (TNF)-alpha
- Interleukin 1 (IL-1) and (IL-6)

Protein kinases:
- Mitogen-activated protein kinases (MAPKs and Akt)

Molecular Promiscuity
Curcumin Has Poor Bioavailability

- Low circulating levels in plasma
- Limited distribution in body tissues
- High levels of phase II conjugated curcuminoids, which have less activity (as opposed to “free” or unchanged curcumin)
- Rapid metabolism
- Short half-life
Enhancing Curcumin Bioavailability

Several technologies have been developed:
- Use of adjuvants such as piperine and cyclodextrin
- Enhanced lipid solubility using liposomes, micelles and phospholipid complexes
- Nanoparticles
- Chemical derivatives of curcumin
- Natural biopolymers eg fenugreek fiber


Image: By LadyofHats (Own work) [Public domain], via Wikimedia Commons

Enhancing Curcumin Bioavailability

Soluble fibre extracted from Fenugreek seed ➔
Galactomannosides
Galactomannosides impregnated with curcuminoids = CGM
CGM greatly enhances bioavailability
CGM increases the percentage of “free curcuminoids” found in plasma compared to conjugated forms (glucuronide & sulfate)
Unconjugated curcuminoids have greater biological activity and can cross membranes and infiltrate tissues


Image: By आशीष भटनागर at Hindi Wikipedia (Own work) [Public domain], via Wikimedia Commons

Evaluating Bioavailability Studies

Design of study: number of participants and use of crossover?
Quality of journal and extent of peer review?
Control dosage used, form and amount?
Free versus conjugated curcuminoids the FCR index?
Undesirable solvents or technology?

FCR = free curcuminoids ratio
Generally human studies using either adjuvants or micelles show increased bioavailability of at best around 6 to 7 times. One study of curcumin with a high dose of piperine did show 20 times, but this was not repeated in other studies that found relatively low enhancements (for example around 2 times).

4 g curcuminoids plus 24 mg piperine, 4 times daily for 4 days. Curcumin, demethoxycurcumin, bisdemethoxycurcumin were not detectable without deconjugation with β-glucuronidase/sulfatase. 8 healthy volunteers.

Curcuminoid Phospholipid Complex. A pharmacokinetic study in 9 healthy volunteers published in 2011 used a high-level design. Curcuminoid conjugates were determined: established that CPC delivered around 30 times (27 to 31) bioavailability compared with curcuminoids alone. However only phase-2 metabolites could be detected.
**CGM Bioavailability Study**

Randomized, double blind, crossover single dose study: curcuminoid galactomannosides (CGM) compared to “straight” curcuminoids (n=50)

- CGM \( \rightarrow \) 45.6 times bioavailability uplift, at a dose of 1000 mg*
- CGM \( \rightarrow \) 24.8 times uplift at a dose of 250 mg**

Bioavailability uplift in terms of free curcuminoids

74% free curcuminoids & 26% conjugated curcuminoids

Suggesting the CGM formulation inhibits initial liver metabolism

* 1000 mg CGM = 391 mg curcuminoids
** 250 mg CGM = 97.7 mg curcuminoids


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**CGM Bioavailability Study**

CGM had a plasma half-life of greater than 3 hours, compared to around 1 hour for straight curcuminoids (slow release)

- \( C_{\text{max}} \) concentrations reached for both doses of CGM were well above the threshold for key pharmacological activities (180 nanomol/L)

Whereas for non-boosted “straight” curcuminoids these levels were never reached

The observed combination of a strong bioavailability uplift with a preservation of the free unconjugated forms was unique


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**CGM and the Blood-brain Barrier**

*An in vivo study confirmed the increased bioavailability of CGM formulation in comparison to unenhanced curcumin*

- Increased distribution of free curcuminoids to heart, liver, kidney, spleen, and in particular, to the brain

Maximum level of free curcuminoids in brain tissues:
- after administration of CGM was 343 ng/g at 2 hours compared to unenhanced curcumin at just 1.4 ng/g
- CGM delivered **245 times** more free curcuminoids!

Unenhanced Curcumin Clinical Trials

Curcumin and Depression

- Meta-analysis of 6 trials, all published 2013 to 2015
- Curcumin dose range → 500 to 2000 mg/day
- 3 trials as adjunctive treatment versus placebo (2 positive)
- 1 trial versus fluoxetine (equivalent)
- 2 trials curcumin versus placebo (1 positive, the other anxiety ↓, not depression)
- Overall curcumin showed a significantly higher reduction in depression symptoms

Curcumin and Prediabetes

- In a randomized, double blind trial (RCT), treatment with curcuminoids (1.5 g/day) prevented the development of type 2 diabetes in prediabetic individuals (0% vs 16.4% (placebo) after 9 months; p<0.001)
- The overall functioning of beta cells was improved in the treated group
- Levels of insulin resistance were also lower in the curcuminoid-treated group at all visits
Curcumin and Inflammation

Curcumin (1.2 g/day) was similar to phenylbutazone and better than placebo in relieving symptoms of postoperative inflammation.

C-reactive protein (CRP) levels on day 3 after surgery were significantly lower in patients undergoing coronary artery bypass grafting who received curcuminoids (4 g/day, 3 days before surgery and for 5 days after), compared to placebo.

CRP levels significantly reduced by 300 mg/day of curcuminoids in type 2 diabetics (RCT of 3 months' duration).

Blood levels of interleukin-6 and tumor necrosis factor-alpha were significantly reduced in patients with type 2 diabetes after treatment with curcuminoids (300 to 600 mg/day of curcumin in RCTs).

Curcumin and Cardiovascular Issues

Curcuminoids (1 g/day) significantly lowered serum triglycerides in obese patients in a double blind, randomized, controlled (RCT) crossover trial.

Treatment with curcuminoids (4 g/day for 8 days) decreased heart attack incidence by more than 50% in patients undergoing coronary bypass surgery.

RCT 82 patients with type 2 diabetes prescribed either 1000 mg of curcuminoids or placebo.

At the end of 12 weeks:

- A significant reduction of serum lipoprotein(a) and an increase in HDL-C concentrations only in the curcuminoid group.
- No significant changes in total cholesterol, LDL-C, and triglycerides in either group.

References:
Curcumin and Pain Management

As well as its anti-inflammatory properties, pharmacological experiments suggest curcumin may interact with opioid, serotonin 1A and TRPA1 receptors.

Curcumin (2 g/day) alleviated postoperative laparoscopic cholecystectomy pain and fatigue in a double blind, placebo-controlled trial (n=50).


Agarwal KA, Tripathi CD, Agarwal BB et al. Surg Endosc 2011; 25(12):3805-3810

Curcumin and Novel Uses

Curcumin (300 mg/day) was clinically effective for patients with Takayasu arteritis (chronic inflammation of the aorta and its main branches).

Curcumin (2 g/day): successful as a replacement for proton pump inhibitor and H2-receptor antagonist drugs in 11 of 14 patients with gastroesophageal reflux (these patients became asymptomatic).

Morgan M. Enhanced Bioavailability: Concentrated Standardised Turmeric Extract Combined with Fenugreek Galactomannosides. A Phytotherapist's Perspective No 159 August 2017

Curcumin and Novel Uses

Curcumin (200 mg/day) for 7 days before and 3 days after menstruation for 3 successive cycles reduced symptoms of premenstrual syndrome in Iranian women; serum levels of brain-derived neurotrophic factor were also significantly higher.

RCT: curcumin (500 mg/day) for 2 months significantly relieved nasal symptoms in patients with seasonal allergic rhinitis.
Bioavailable Curcumin From Turmeric in the Clinic

Clinical Uses as a Primary Herb

Chronic disease prevention and healthy aging, especially in patients generating unhealthy levels of non-resolving inflammation
For any condition being fed by neuroinflammation such as low mood, complex brain disorders, dementia, chronic fatigue syndrome etc.
Type 2 diabetes, prediabetes and especially for reducing the microangiopathy
Clinical Uses as a Primary Herb

Pain management linked to inflammation
Cardiovascular risk management, including lowering lipids and vascular inflammation
General support for autoimmunity

Clinical Uses as a Secondary Herb

Osteoarthritis
Inflammatory bowel disease
Non-alcoholic fatty liver disease (NAFLD)
Clinical antioxidant activity via Nrf2/ARE activation and other effects, leading to detoxification (including for heavy metals) and for after coronary bypass surgery
Microcirculatory and eye and kidney health
Others including gastroesophageal reflux, HIV-associated diarrhea, chronic skin conditions; BPH

Bioavailable Curcumin from Turmeric (BCT) Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Primary Herbs</th>
<th>Secondary Herbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation/Pain</td>
<td>BCT</td>
<td>Boswellia, Willow bark, Gotu Kola</td>
</tr>
<tr>
<td>(eg disc prolapse, injury)</td>
<td>Horsechestnut, BCT</td>
<td>Boswellia, Gotu Kola</td>
</tr>
<tr>
<td>Soft tissue injury</td>
<td>Horsechestnut, BCT</td>
<td>Rosemary, Green Tea, Grape seed</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>Gymnema, BCT</td>
<td>Polygonum (Fallopia)</td>
</tr>
<tr>
<td>Prediabetes</td>
<td>BCT, Gymnema</td>
<td>Silymarin</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>BCT, Gymnema</td>
<td></td>
</tr>
</tbody>
</table>
### Bioavailable Curcumin Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Primary Herbs</th>
<th>Secondary Herbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic complications</td>
<td>Gotu Kola, Grape Seed, BCT</td>
<td></td>
</tr>
<tr>
<td>CVD risk management</td>
<td>BCT</td>
<td>Rosemary, Green Tea, Grape Seed</td>
</tr>
<tr>
<td>Autoimmune (general)</td>
<td>BCT</td>
<td></td>
</tr>
<tr>
<td>Neuroinflammatory states</td>
<td>Boswellia, BCT</td>
<td></td>
</tr>
<tr>
<td>Chronic skin conditions</td>
<td>BCT</td>
<td></td>
</tr>
</tbody>
</table>

### Bioavailable Curcumin Indications

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<thead>
<tr>
<th>Indication</th>
<th>Primary Herbs</th>
<th>Secondary Herbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>Boswellia</td>
<td>BCT, Gotu Kola</td>
</tr>
<tr>
<td>IBD</td>
<td>Boswellia</td>
<td>BCT</td>
</tr>
<tr>
<td>NRF2/Detox/Antioxidant Activity</td>
<td>Rosemary, Green Tea, Grape seed, normal Turmeric</td>
<td>BCT</td>
</tr>
<tr>
<td>Stress</td>
<td>Rhodiola, Korean Ginseng, Schisandra</td>
<td>BCT</td>
</tr>
<tr>
<td>Liver detox</td>
<td>Rosemary, Silymarin, Schisandra, normal Turmeric</td>
<td>BCT</td>
</tr>
</tbody>
</table>

### Concluding Remarks

A new innovation based on a natural curcuminoid-impregnated soluble fiber microgranulate is a significant breakthrough for natural therapists. Because of the molecular promiscuity of curcumin and the way that non-resolving inflammation feeds most chronic disease processes, its potential uses are myriad. Network pharmacological considerations suggest that we can achieve a high clinical potency with a minimal risk of side effects.
The greatest use of your time

Think New Thoughts

Change the world

It wants to