FUNCTIONAL MEDICINE
Continuing Education

Building Immunity: Dispensing the Dietary& Nutraceutical Prescription

Lara Zakaria RPh MS CNS CDN IFMCP
Hello@LaraZakaria.com
@foodiefarmacist

Partners

- *Financial support was provided for this course through an educational grant from KBMO Diagnostics and Your Financial Pharmacist.*

Disclosures

- Lara Zakaria does not report any actual or potential conflicts of interest in relation to this continuing pharmacy education course.

Objectives

1. Discuss dietary and lifestyle modifications for balancing immune response and decreasing inflammation
2. Review nutraceutical products for immune modulation

Decide once and for all …

Feed a cold, starve a fever?

And…

Does alcohol really kill an infection?

Today's Outline

Foundations of the dietary approach	Macronutrients
	Micronutrients
	Phytonutrients
Where's the evidence?	Anti-inflammatory diets
	Meal timing considerations
Building the prescription	Limitations of diet
	Nutraceuticals

"You are completely free to carry out whatever research you want, so long as you come to these conclusions."

THE CONVERSATION

Academic rigor, journalistic flair

COVID-19 Arts + Culture Economy + Business Education Environment + Energy Ethics + Religion Health Politics/Election '20

Coronavirus: there are no miracle diets that can prevent or cure CO

April 21, 2020 5.41am EDT

Cedars-Sinai Blog

Can You Really Boost Your Immune System?

Jun 01, 2020 *Cedars-Sinai Staff*

SHARE TWEET POST

The idea of boosting your immune system is appealing, but is it even possible to build up your immune system so that you rarely get sick?

Dr. Suzanne Cassel, an immunologist at Cedars-Sinai, says that the concept of boosting your immune system is inaccurate. There's also widely held confusion about how your immune system functions and how your body is designed to combat diseases and infections.

"You actually don't want your immune system to be stronger, you want it to be balanced."

nutrients

MDPI

Review

COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation

Ioannis Zabetakis [1,2,*], Ronan Lordan [2,3], Catherine Norton [2,4] and Alexandros Tsoupras [1,2]

Received: 22 April 2020; Accepted: 17 May 2020; Published: 19 May 2020

check for updates

Abstract: The novel coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has engulfed the world, affecting more than 180 countries. As a result, there has been considerable economic distress globally and a significant loss of life. Sadly, the vulnerable and immunocompromised in our societies seem to be more susceptible to severe COVID-19 complications. Global public health bodies and governments have ignited strategies and issued advisories on various handwashing and hygiene guidelines, social distancing strategies, and, in the most extreme cases, some countries have adopted "stay in place" or lockdown protocols to prevent COVID-19 spread. Notably, there are several significant risk factors for severe COVID-19 infection. These include the presence of poor nutritional status and pre-existing noncommunicable diseases (NCDs) such as diabetes mellitus, chronic lung diseases, cardiovascular diseases (CVD), obesity, and various other diseases that render the patient immunocompromised. These diseases are characterized by systemic inflammation, which may be a common feature of these NCDs, affecting patient outcomes against COVID-19. In this review, we discuss some of the anti-inflammatory therapies that are currently under investigation intended to dampen the cytokine storm of severe COVID-19 infections. Furthermore, nutritional status and the role of diet and lifestyle is considered, as it is known to affect patient outcomes in other severe infections and may play a role in COVID-19 infection. This review speculates the importance of nutrition as a mitigation strategy to support immune function amid the COVID-19 pandemic, identifying food groups and key nutrients of importance that may affect the outcomes of respiratory infections.

Nutrients. 2020;12(5):1466

Mediterranean diet vs SAD

- Fruits and veg
- Fish oil
- Vitamin C
- Vitamin D
- Vitamin E
- Zinc
- Copper
- Fiber

Functional Medicine Prescription

Patient Name_____ Date of Birth _____

Functional Nutrition Prescription

Functional Nutrition
- ☐ Phytonutrient Spectrum
- ☐ Core Food Plan (CFP)
- ☐ CFP, modified: _____

First Step Interventions
- ☐ Elimination Diet
- ☐ Food Reintroduction
- ☐ Cardiometabolic Food Plan

Advanced Interventions
- ☐ GI Specific Food Plans
- ☐ Detox Food Plan
- ☐ Mito Food Plan

Personal Dietary Recommendations

Macronutrient Distribution: ☐ 45/25/30 ☐ 40/30/30 ☐ Mild/Strict Keto ☐ Intermittent Fasting _____ days/wk

Target Calories: ☐ 600 ☐ 1000–1200 ☐ 1200–1400 ☐ 1400–1800 ☐ 1800–2200 ☐ 2200–2500

_____

_____

Lifestyle Prescription

☐ **Sleep:** _____

☐ **Exercise:** Risk Assessment: ☐ Low Risk ☐ Medium Risk ☐ High Risk

Clearance: ☐ Yes ☐ No _____

Exercise Prescription:	Cardio/Aerobic	Strength/Resistance	Flexibility/Stretching	Balance
F – Frequency times per week				
I – Intensity (e.g., low, moderate, vigorous)				
T - Time/duration minutes each day				
T - Type (e.g., walking, jogging, swimming)				

☐ **Stress management:** _____

Supplements/Medications Prescription

Supplement/ Medication	On rising	Breakfast	Mid-morning	Lunch	Mid-afternoon	Dinner	Mid-evening	Before bed

Additional Comments _____

_____

Prescribed by _____ Date _____

Follow-up Appointment _____

VS

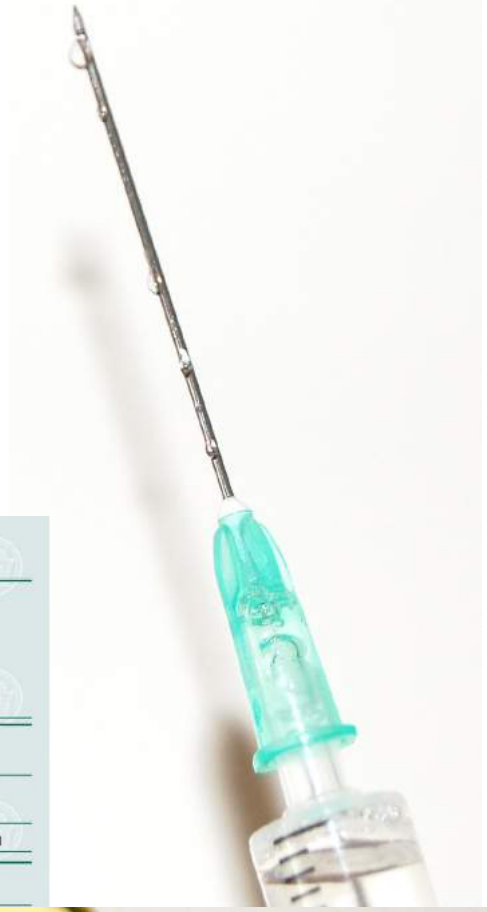
State of New Jersey
PRESCRIPTION BLANK

NAME AND TITLE
STREET
CITY STATE ZIP
PHONE

NPI # _____
CERTIFICATION # 11111 DEA # 11111
COLLABORATING PHYSICIAN
NAME NAME LICENSE # 00000000
(Enter Address and Phone Number only if different from above)
ADDRESS STREET ADRESS
CITY, STATE ZIP CODE PHONE # (000) 000-0000

PATIENT _____ D.O.B. _____
ADDRESS _____ DATE _____
Rx

SUBSTITUTION PERMISSIBLE _____ DO NOT SU
DO NOT REFILL _____ SIGNATURE OF PRESCRIBER
REFILL _____ TIMES
Use a separate form for each controlled substance pres
THEFT, UNAUTHORIZED POSSESSION AND/OR USE OF THIS FORM INCLUDING ALTERATIONS OR FORGER



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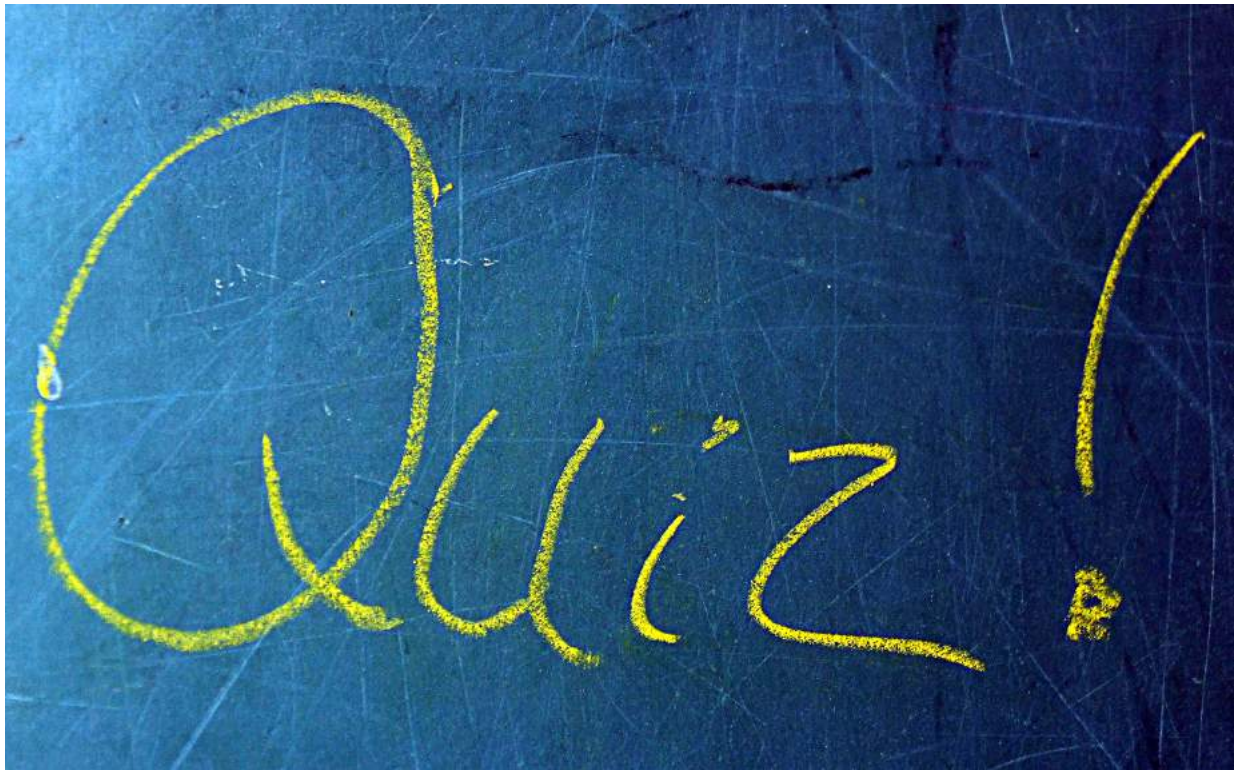
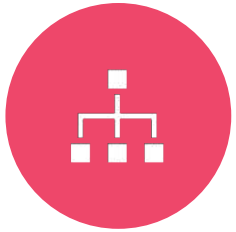
Let’s test our foundational knowledge



Inflammation: The Functional Medicine Window



SY*STEM'S* BASED APPROACH

UPSTREAM MEDICINE

VS

"SY*MPTOM*-BASED" APPROACH

DOWNSTREAM MEDICINE

Macronutrients, Micronutrients, & Phytonutrients

Foundations of the Nutrition Prescription

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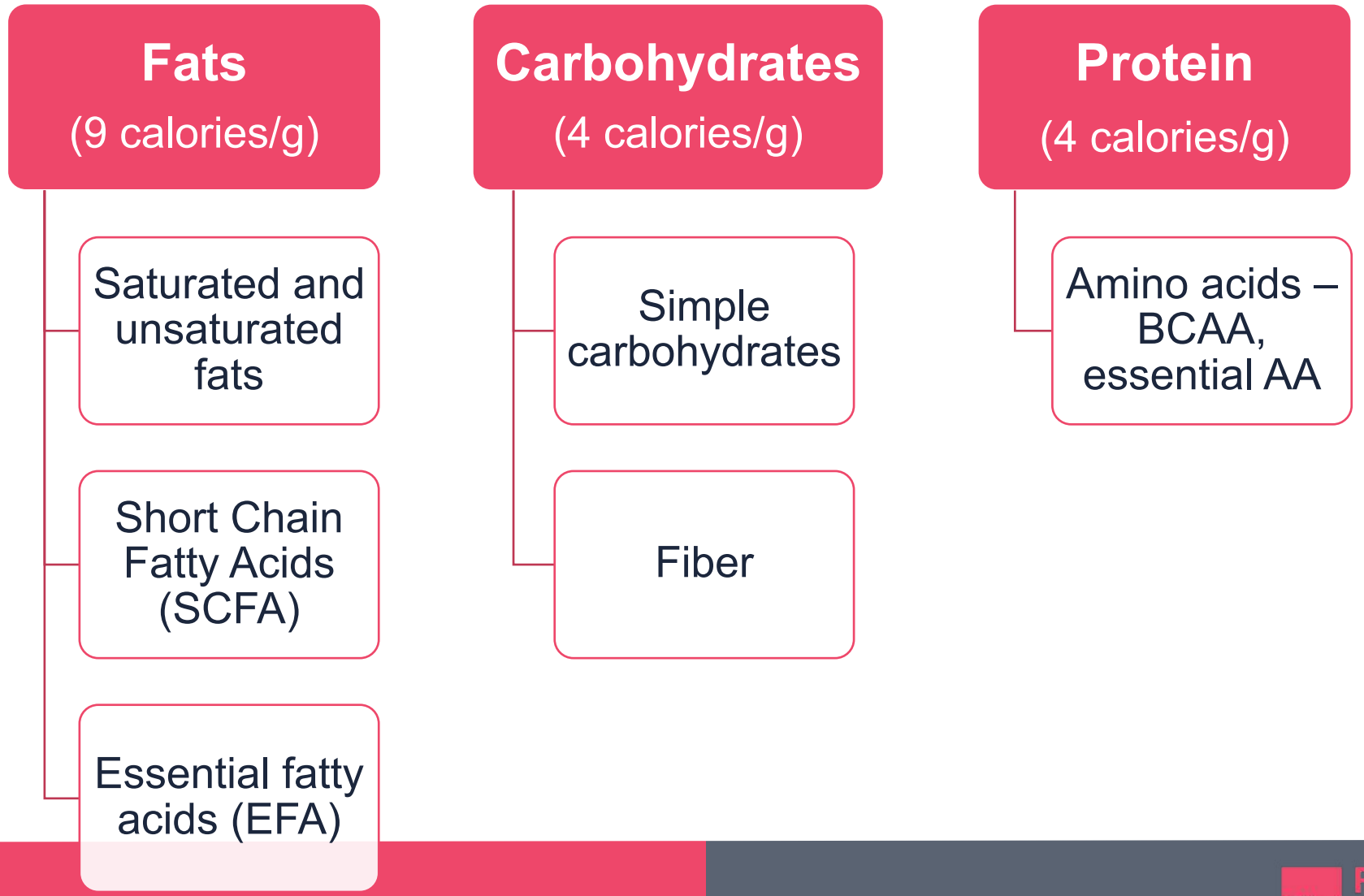
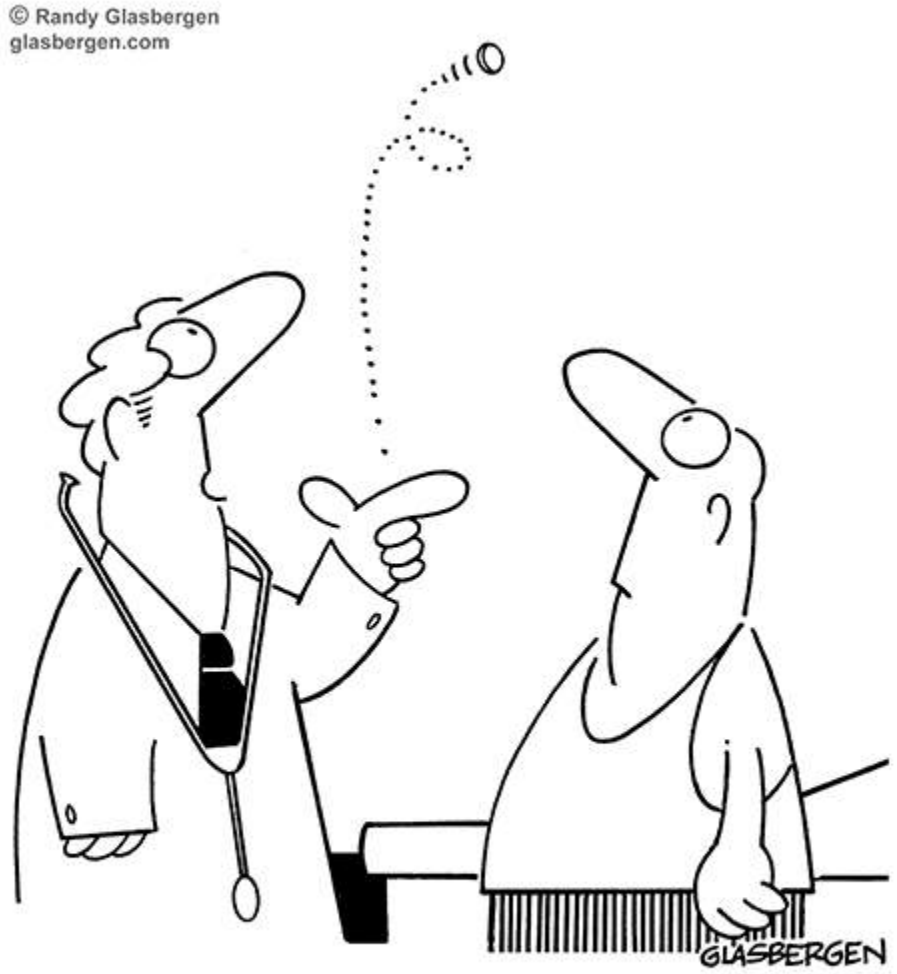
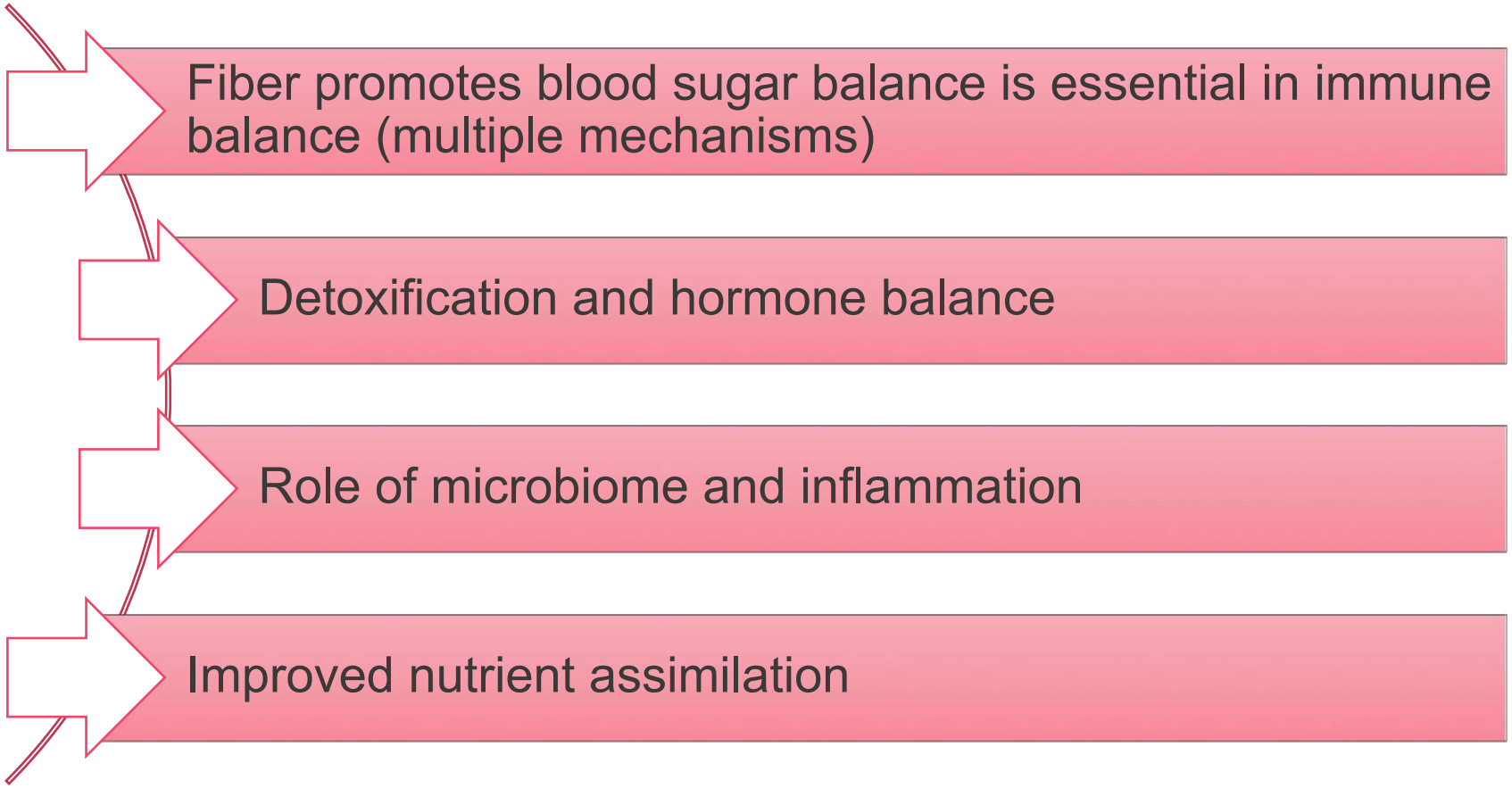
Macronutrients





**"Heads, fat is bad and carbs are good.
Tails, fat is good and carbs are bad."**

The Importance of Fiber



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6472268/

The Standard American Diet

SAD ☹

PLOS ONE

RESEARCH ARTICLE

Activation of the Nrf2 Cell Defense Pathway by Ancient Foods: Disease Prevention by Important Molecules and Microbes Lost from the Modern Western Diet

Donald R. Senger[1,2]*, Dan Li[1], Shou-Ching Jaminet[1,2], Shugeng Cao[3]

1 Department of Pathology and Center for Vascular Biology Research, Beth Israel Dea Center, Boston, Massachusetts, United States of America, 2 Department of Pathology School, Boston, Massachusetts, United States of America, 3 Department of Pharmace Daniel K. Inouye College of Pharmacy, University of Hawaii at Hilo, Hilo, Hawaii, Unite

* dsenger@bidmc.harvard.edu

Abstract

The Nrf2 (NFE2L2) cell defense pathway protects against oxidative stres including cancer and neurodegeneration. Although activated modestly b alone, robust activation of the Nrf2 defense mechanism requires the add co-factors that facilitate electron exchange. Various molecules exhibit thi tion, including sulforaphane from cruciferous vegetables. However, natura are potent and widely available from dietary sources have not been identified previously. The objectives of this study were to investigate support of the Nrf2 cell defense pathway by the alkyl catechols: 4-methylcatechol, 4-vinylcatechol, and 4-ethylcatechol. These small electrochemicals are naturally available from numerous sources but have not received attention. Findings reported here illustrate that these compounds are indeed potent co-factors for activation of the Nrf2 pathway both *in vitro* and *in vivo*. Each strongly supports expression of Nrf2 target genes in a variety of human cell types; and, in addition, 4-ethylcatechol is orally active in mice. Furthermore, findings reported here identify important and previously unrecognized sources of these compounds, arising from biotransformation of common plant compounds by lactobacilli that express phenolic acid decarboxylase. Thus, for example, *Lactobacillus plantarum*, *Lactobacillus brevis*, and *Lactobacillus collinoides*,

[The] absence of alkyl catechols from the modern Western diet suggests serious negative consequences for Nrf2 cell defense, resulting in reduced protection against multiple chronic diseases associated with oxidative stress.

Most Americans do not meet the minimum RDA recommendations ~30 g per day (men 38 g and women 25 g)

PLoS One. 2016;11(2):e0148042

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PLOS | ONE

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Donald R. Senger[1,2]*, Dan Li[1], Shou-Ching Jaminet[1,2], Shugeng Cao[3]

Phenolic acid decarboxylase (PAD) is pivotal to the generation of these Nrf2 co-factors.

PAD is expressed by a subset of lactobacillus species and associated with a variety of plant-based foods including those traditionally fermented including (fermented) olives, cabbage, cucumbers, eggplants, caper berries,grape extracts, sourdough bread, ciders, wines, and whiskeys

PLoS One. 2016;11(2):e0148042

Nrf2: Detoxification & Antioxidant

The Nrf2-mediated signaling pathway protection against environmental insults and endogenous stressors.

Nrf2 coordinates inducible expression of antioxidant responsive element (ARE) and phase II detoxification enzymes to adapt to different stress conditions

Nrf2 raising factors include **hormesis, exercise and caloric restriction**

J Nutr Biochem. 2015;26(12):1401–1413
Sheng Li Xue Bao. 2015 Feb 25;67(1):1-18

JASN Journal of the American Society of Nephrology

Role of High Glucose–Induced Nuclear Factor–κB Activation in Monocyte Chemoattractant Protein-1 Expression by Mesangial Cells

HUNJOO HA,* MI RA YU,* YOON JIN CHOI,* MASANORI KITAMURA,† and HI BAHL LEE*

*Hyonam Kidney Laboratory, Soon Chun Hyang University, Seoul, Korea; and †University College London Medical School, The Rayne Institute, London, United Kingdom.

Abstract. Although high glucose (HG) has been shown to induce nuclear factor–κB (NF-κB) activation in vascular cells, the upstream regulation and the biologic significance of NF-κB activation in diabetic renal injury are not clear. It was, therefore, examined if HG-induced generation of reactive oxygen species (ROS) and protein kinase C (PKC) activation are involved in NF-κB activation in mesangial cells (MC), and the role of NF-κB activation in HG-induced monocyte chemoattractant protein-1 (MCP-1) expression by MC was further investigated. Recent observations suggest that MCP-1 may play a role in the development and progression of diabetic nephropathy. HG rapidly induced NF-κB activation in MC as estimated by electrophoretic mobility shift assay. Supershift assay suggests that most of the binding activity arose from p50/p50 and p50/p65 dimers. Antioxidants, pyrrolidine dithiocarbamate, N-acetyl-L-cystein, and trolox effectively inhibited HG-induced NF-κB activation in MC. HG rapidly generated dichlorofluorescin-sensitive intracellular ROS in MC as measured by laser-scanning confocal microscopy. HG also activated PKC rapidly in MC. Inhibi… of PKC effectively blocked HG-induced intracellula… activation in MC. HG increased … 1.9-fold and protein secretion by … cose in MC transfected with c… transfected with dominant negati… (IκBαM). Inhibition of either PK… HG-induced, but not basal, MC… transfected with control vector. … that HG rapidly activates NF-κB i… and suggests that HG-induced NF-κB activation in MC may play a role in diabetic renal injury through upregulation of MCP-1 mRNA and protein expression.

High glycemic diet activates NF-kB via protein kinase C (PKC) and reactive oxygen species (ROS)

J Am Soc Nephrol. 2002 Apr;13(4):894-902

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Promoting Nrf2: Glycemic Impact

- Reduce or avoid sugar, sweetened beverages, or white flour products
- Eat unprocessed foods in natural state
- Increase overall consumption from:
  - Vegetables
  - Fruit
  - Whole grains
  - Legumes
- Couple with protein and healthy fat sources (avocado, nuts, seeds, etc…)

Promoting Nrf2: Specific Nutrients & Other Factors

Nutrients that promote Nrf2:

- Phenolic antioxidants
- Vitamin E (gamma- and delta-tocopherols and tocotrienols)
- Omega-3 FA (DHA and EPA)
- Vitamin A (Carotenoids, lycopene)
- Isothiocyanates from cruciferous vegetables
- Sulfur compounds from allium vegetables
- Terpenoids.

Other Nrf2 promoting factors:

- Low level oxidative stress (hormesis)
- Exercise
- Caloric restriction.(IF, FMD, fasting)

J Nutr Biochem. 2015;26(12):1401–1413
Sheng Li Xue Bao. 2015 Feb 25;67(1):1-18

Advanced Glycation End Products (AGEs)

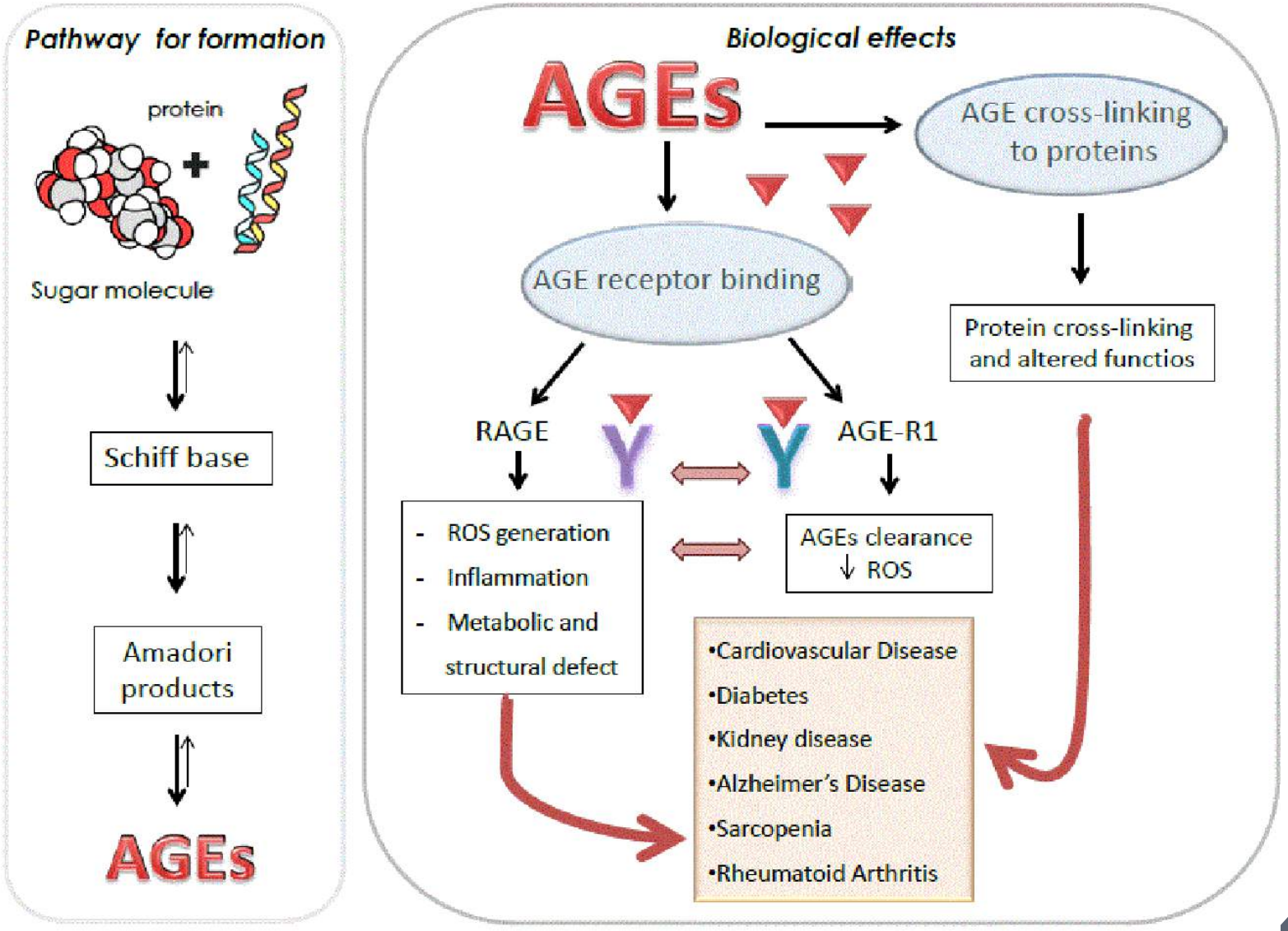


Figure 1: Schematic representation of AGEs formation and of their biological effects.

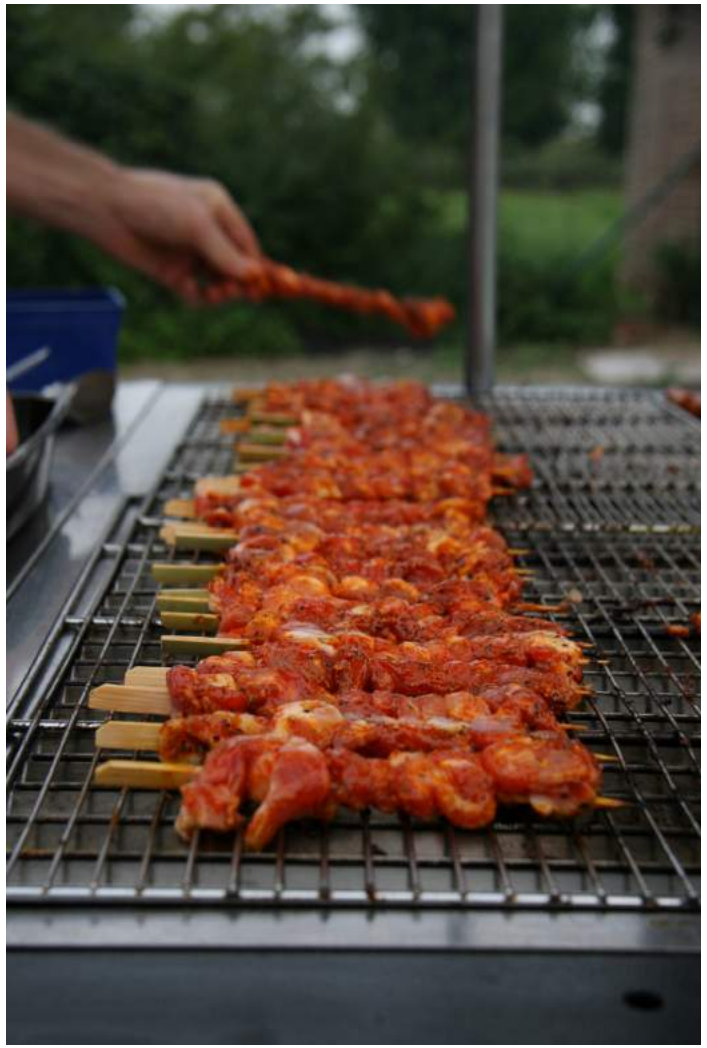
J Diabetes. 2020 Feb;12(2):102-104

AGEs: Cooking Methods

Dry heat cooking increases AGEs significantly

Due to barbecuing, grilling, roasting, baking, frying, sautéing, broiling, searing, and toasting

Animal-source foods (including meat, cheeses, fried eggs, butter, cream cheese, margarine, mayonnaise) and highly processed food products are most susceptible to elevations in AGEs due to high fat and protein, in combination to high heat cooking



Meats and meat substitutes	AGE Content		
	AGE kU/100 g	Serving size (g)	AGE kU/serving
Beef			
Beef, bologna	1,631	90	1,468
Beef, corned brisket, deli meat (Boar's Head, Sarasota, FL)	199	90	179
Beef, frankfurter, boiled in water, 212° F, 7 min	7,484	90	6,736
Beef, frankfurter, broiled 450°F, 5 min	11,270	90	10,143
Beef, ground, boiled, marinated 10 min w/lemon juice	1,538	90	1,384
Beef, ground, pan browned, marinated 10 min w/lemon juice	3,833	90	3,450
Beef, ground, 20% fat, pan browned	4,928	90	4,435
Beef, ground, 20% fat, pan/cover	5,527	90	4,974
Beef, hamburger (McDonald's Corp[d], Oak Brook, IL)	5,418	90	4,876
Beef, hamburger patty, olive oil 180°F, 6 min	2,639	90	2,375
Beef, meatball, potted (cooked in liquid), 1 h[c]	4,300	90	3,870
Beef, meatball, w/sauce[c]	2,852	90	2,567
Beef, meatloaf, crust off, 45 min	1,862	90	1,676
Beef, raw	707	90	636
Beef, roast[b]	6,071	90	5,464
Beef, salami, kosher (Hebrew National, ConAgra Foods, Omaha, NE)	628	90	565
Beef, steak, broiled[c]	7,479	90	6,731
Beef, steak, grilled 4 min, George Foreman grill (Salton Inc, Lake Forest, IL)	7,416	90	6,674
Beef, steak, microwaved, 6 min	2,687	90	2,418
Beef, steak, pan fried w/olive oil	10,058	90	9,052

Fish/seafood			
Crabmeat, fried, breaded (take out)	3,364	90	3,028
Fish, loaf (gefilte), boiled 90 min	761	90	685
Salmon, Atlantic, farmed, prev. frozen, microwaved, 1 min, high heat[c]	954	90	859
Salmon, Atlantic, farmed, prev. frozen, poached, 7 min, medium heat[c]	1,801	90	1,621
Salmon, Atlantic, farmed, prev. frozen, steamed, 10 min, medium heat[c]	1,212	90	1,091
Salmon, Atlantic, farmed, prev. frozen, steamed in foil, 8 min, medium heat[c]	1,000	90	900
Salmon, breaded, broiled 10 min	1,498	90	1,348
Salmon, broiled with olive oil	4,334	90	3,901
Salmon, canned pink (Rubenstein, Trident Seafoods, Seattle, WA)	917	90	825
Salmon, fillet, boiled, submerged, 18 min	1,082	90	974
Salmon, fillet, broiled	3,347	90	3,012
Salmon, fillet, microwaved	912	90	821
Salmon, fillet, poached	2,292	90	2,063
Salmon, pan fried in olive oil	3,083	90	2,775
Salmon, raw, previously frozen	517	90	465
Salmon, raw	528	90	475
Salmon, smoked	572	90	515

Reducing AGEs

Moist cooking methods may decrease the formation of AGEs. These methods include poaching, simmering, boiling, braising, stewing, pot roasting, steaming, and sous vide (LTLT).

Acidic pH arrests AGE development; Marinades with lemon juice and vinegar 1 hour prior to cooking

Reduce intake of highest AGE foods; from highest to lowest beef and cheeses rank highest, followed by poultry, pork, fish, and eggs note that lamb ranked relatively low compared to other animal meats

Neutralize ROS activation by increasing intake of antioxidant rich foods

J Am Diet Assoc. 2010;110(6):911-16.e12
https://www.nytimes.com/wirecutter/reviews/best-sous-vide-gear/

www.nature.com/scientificreports

OPEN

Integrated metabolomic and transcriptome analyses reveal finishing forage affects metabolic pathways related to beef quality and animal welfare

Received: 14 September 2015
Accepted: 18 April 2016
Published: 17 May 2016

José A. Carrillo[1], Yanghua He[1], Yaokun Li[2], Jianan Liu[1], Richard A. Erdman[1], Tad S. Sonstegard[3] & Jiuzhou Song[1]

Sci Rep. 2016;6:25948. Published 2016 May 17. doi:10.1038/srep25948
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4869019/

Quality Matters: Grass-Fed *and* Finished

Grass-fed and finished beef:

- Omega-3 FA are higher
- Produce tender beef with lower total fat and a higher omega3/omega6 (favorable) ratio than grain-fed ones
- Reduction in direct markers of inflammation as well as indirect benefit health

Grain finished/conventionally raised animals

- Omega-6 FA in are higher and may promote inflammation and oxidative stress.

Bonus: Reduce blood cortisol levels in the animal strongly indicate that grass-fed animals may experience less stress than the grain-fed ones.

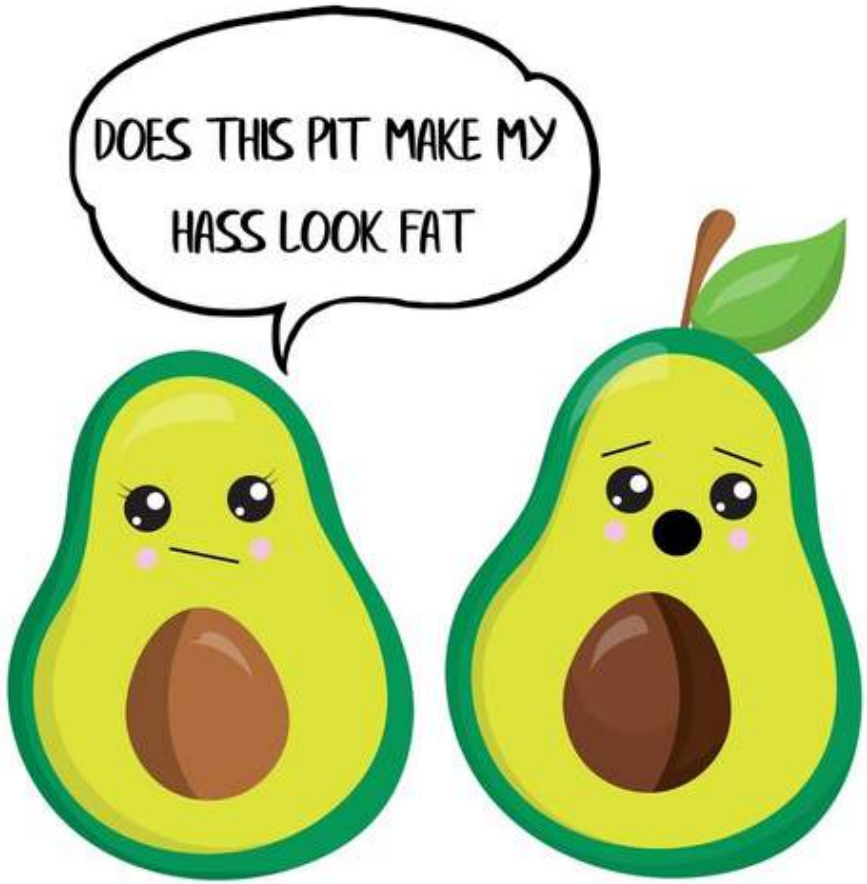
Some evidence also suggests improved CO_2 gas emission (less methane production)

Sci Rep. 2016;6:25948. Published 2016 May 17. doi:10.1038/srep25948
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4869019/

The Misunderstood Macronutrient: Fats

Benefits of healthy fats like avocado and olives associated with:

- Improved blood sugar balance
- Favorable modulation of the microbiome
- Phytochemicals known to modulate immune response



Fats

- Fatty Acids
  - Saturated
    - Lauric acid
    - Myristic acid
    - Palmitic acid
    - Stearic acid
  - Unsaturated
    - Monounsaturated (MUFA)
      - Oleic acid (Omega 9)
    - Polyunsaturated (PUFA)
      - Omega 6 (O6)
        - Linoleic acid
        - CLA
        - GLA
        - Arachidonic acid (AA)
      - Omega 3 (O3)
        - Linolenic acid
        - EPA
        - DHA

Pro- vs Anti-inflammatory fats: PUFAs

Proinflammatory PUFAs

- Omega-6 fats (nuts, seeds, grains, processed foods)
- Arachidonic acid (AA) (egg, meat, dairy*)
- Linoleic acid (corn, sunflower, and safflower oils)

Anti-inflammatory PUFAs

- Omega-3 fats (fatty fish, fish oil)
- Alpha linoleic acid (ALA)

Ratio of Omega-6/Omega 3 in SAD ~ 15-20:1

Ideal ratio 4:1

**grass-fed and organic sources have been found to have reduced AA compared to conventional sources*

Guilliams TG. Supporting Immune Function:
A Lifestyle and Nutrient Approach. 2014 p78

The Forgotten Macronutrient: Water

Drink clean filtered water, free of contaminants

½ body weight (lbs to oz) (the “pee test”)

Other sources include veggies, fruit, soup, herbal teas, carbonated water (not tonic)

Caffeine and alcohol are dehydrating

Hydrate more when physical demands are higher, exercise, or the weather is hot

Micronutrients

- Vitamins
- Minerals
- Functionally Essential Nutrients
- Antioxidants

Nutrients involved in immune balance

- Vitamin C
- Vitamin A and beta-carotene
- Vitamin D
- Vitamin E (other antioxidants like Selenium)
- Zinc

Nutrients involved in immune balance

Detoxification and antioxidant support, including methylation, sulfation, glutathione production co-factors

- Lipoic acid
- NAC
- Glutathione

Mitochondrial support/Oxidative stress

- CoQ10
- Carnitine

Research

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

BMJ 2017 ; 356 doi: https://doi.org/10.1136/bmj.i6583 (Published 15 February 2017)
Cite this as: *BMJ* 2017;356:i6583

Abstract

Objectives To assess the overall effect of vitamin D supplementation on risk of acute respiratory infection, and to identify factors modifying this effect.**Design** Systematic review and meta-analysis individual participant data (IPD) from randomised controlled trials.**Data sources** Medline, Embase, the Cochrane Central Register of Controlled Trials, Web of Science, ClinicalTrials.gov, and the International Standard Randomised Controlled Trials Number registry from inception to December 2015.**Eligibility criteria for study selection** Randomised, double blind, placebo controlled trials of supplementation with vitamin D_3 or vitamin D_2 of any duration were eligible for inclusion if they had been approved by a research ethics committee and if data on incidence of acute respiratory tract infection were collected prospectively and prespecified as an efficacy outcome.**Results** 25 eligible randomised controlled trials (total 11 321 participants, aged 0 to 95 years) were identified. IPD were obtained for 10 933 (96.6%) participants. Vitamin D supplementation reduced the risk of acute respiratory tract infection among all participants (adjusted odds ratio 0.88, 95% confidence interval 0.81 to 0.96; P for heterogeneity <0.001). In subgroup analysis, protective effects were seen in those receiving daily or weekly vitamin D without additional bolus doses (adjusted odds ratio 0.81, 0.72 to 0.91) but not in those receiving one or more bolus doses (adjusted odds ratio 0.97, 0.86 to 1.10; P for interaction=0.05). Among those receiving daily or weekly vitamin D, protective effects were stronger

Vitamin D supplementation significantly and safely **reduced the risk of general respiratory infection**

BMJ. 2017 Feb 15;356:i6583

Vitamin D Mechanisms

Cellular defense and repair

- Activates immune cells
- Stimulates anti-microbial molecules
- May reduce cytokine storm

Interrupts virus effects

- Reduces virus-triggered messenger molecules
- Reduces virus replication

nutrients

MDPI

Review

Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths

William B. Grant [1,*], Henry Lahore [2], Sharon L. McDonnell [3], Carole A. Baggerly [3], Christine B. French [3], Jennifer L. Aliano [3] and Harjit P. Bhattoa [4]

Received: 12 March 2020; Accepted: 31 March 2020; Published: 2 April 2020

check for updates

Abstract: The world is in the grip of the COVID-19 pandemic. Public health measures that can reduce the risk of infection and death in addition to quarantines are desperately needed. This article reviews the roles of vitamin D in reducing the risk of respiratory tract infections, knowledge of the epidemiology of influenza and COVID-19, and how vitamin D supplementation might be a useful measure to reduce risk. Through several mechanisms, vitamin D can reduce risk of infection. Those mechanisms include inducing cathelicidins and defensins that can lower viral replication rates and reducing concentrations of pro-inflammatory cytokines that produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increasing concentrations of anti-inflammatory cytokines. Several observational studies and clinical trials reported that vitamin D supplementation reduced the risk of influenza, whereas others did not. Evidence supporting the role of vitamin D in reducing risk of COVID-19 includes that the outbreak occurred in winter, a time when 25-hydroxyvitamin D (25(OH)D) concentrations are lowest; that the number of cases in the Southern Hemisphere near the end of summer are low; that vitamin D deficiency has been found to contribute to acute respiratory distress syndrome; and that case-fatality rates increase with age and with chronic disease comorbidity, both of which are associated with lower 25(OH)D concentration. To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/d of vitamin D_3 for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/d. The goal should be to raise 25(OH)D concentrations above 40–60 ng/mL (100–150 nmol/L). For treatment of people who become infected with COVID-19, higher vitamin D_3 doses might be useful. Randomized controlled trials and large population studies should be conducted to evaluate these recommendations.

To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/d of vitamin D_3 for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/d. The goal should be to raise 25(OH)D concentrations above 40–60 ng/mL (100–150 nmol/L).

Nutrients. 2020 Apr 2;12(4):988

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ORIGINAL ARTICLE

Vitamin D deficiency contributes directly to the acute respiratory distress syndrome (ARDS)

Rachel C A Dancer,[1] Dhruv Parekh,[1] Sian Lax,[1] Vijay D'Souza,[1] Shengxing Zheng,[1] Chris R Bassford,[1] Daniel Park,[1] D G Bartis,[1] Rahul Mahida,[1] Alice M Turner,[1] Elizabeth Sapey,[1] Wenbin Wei,[2] Babu Naidu,[1] Paul M Stewart,[3] William D Fraser,[4] Kenneth B Christopher,[5] Mark S Cooper,[6] Fang Gao,[1] David M Sansom,[7] Adrian R Martineau,[8] Gavin D Perkins,[9] David R Thickett[1]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2014-206680).

For numbered affiliations see end of article.

Correspondence to
Professor David Thickett, Centre for Translational Inflammation and Fibrosis Research, Queen Elizabeth Hospital, University of Birmingham, Birmingham B15 2TH, UK;
d.thickett@bham.ac.uk

RCAD and DP are joint first author of this paper.

Received 10 December 2014
Revised 10 March 2015
Accepted 2 April 2015

ABSTRACT

Rationale Vitamin D deficiency has been implicated as a pathogenic factor in sepsis and intensive therapy unit mortality but has not been assessed as a risk factor for acute respiratory distress syndrome (ARDS). Causality of these associations has never been demonstrated.

Objectives To determine if ARDS is associated with vitamin D deficiency in a clinical setting and to determine if vitamin D deficiency in experimental models of ARDS influences its severity.

Methods Human, murine and in vitro primary alveolar epithelial cell work were included in this study.

Findings Vitamin D deficiency (plasma 25(OH)D levels <50 nmol/L) was ubiquitous in patients with ARDS and present in the vast majority of patients at risk of developing ARDS following oesophagectomy. In a murine model of intratracheal lipopolysaccharide challenge, dietary-induced vitamin D deficiency resulted in exaggerated alveolar inflammation, epithelial damage and hypoxia. In vitro, vitamin D has trophic effects on primary human alveolar epithelial cells affecting >600

Key messages

What is the key question?

► Is vitamin D deficiency a risk factor for the development of acute respiratory distress syndrome (ARDS)?

What is the bottom line?

► Patients with and at risk of ARDS are highly likely to be deficient, and severity of vitamin D deficiency relates to increased epithelial damage, the development of ARDS and survival.

Why read on?

► We present evidence that an easily treatable vitamin deficiency may increase the risk of ARDS in patients at risk.

Vitamin D deficiency (defined as plasma 25(OH)D levels <50 nmol/L) was present in the vast majority of patients at risk of developing ARDS

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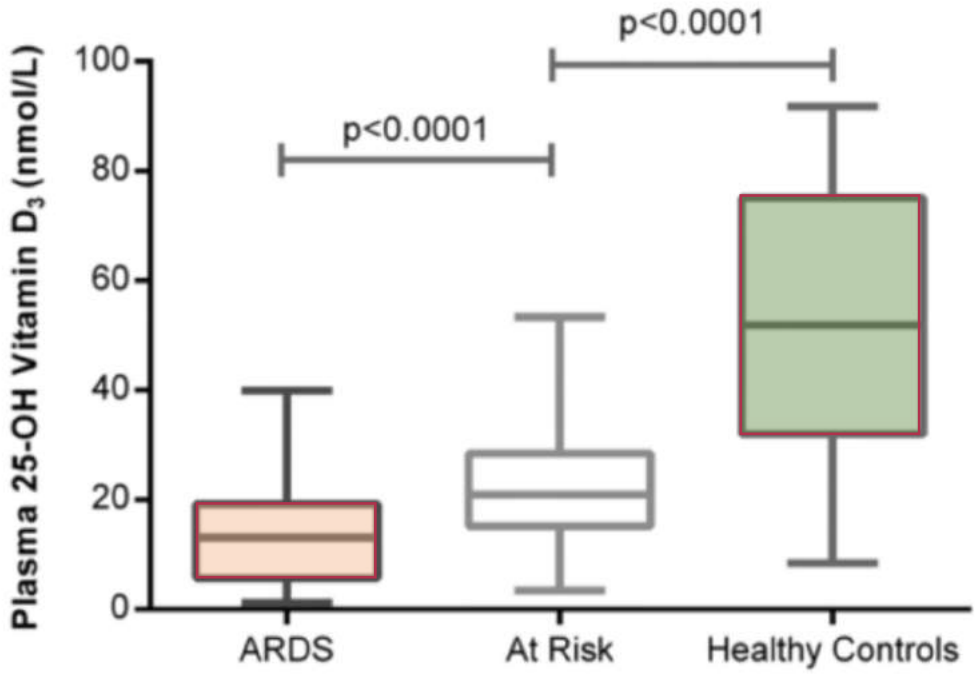
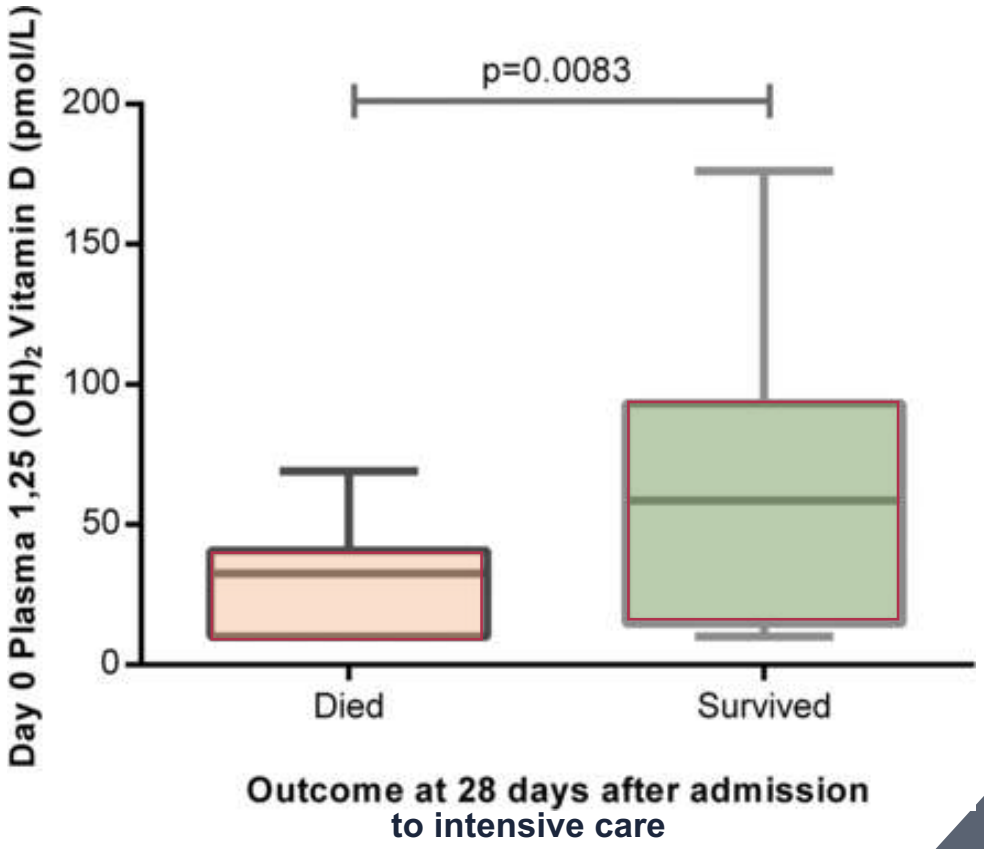
Vitamin D deficiency contributes directly to the acute respiratory distress syndrome (ARDS)





Thorax. 2015 Jul;70(7):617-24

Vitamin D Supplementation Dosing

Adults

- 2000-5000 IU/day

Children

- Age-based dosing
- Infants & toddlers 400-1,000 IU/day
- 600-1,000 IU/day children and adolescents

Ideally, test don’t guess

Linus Pauling Institute. LPI https://lpi.oregonstate.edu/mic/vitamins/vitamin-D

N-Acetyl Cysteine (NAC)

Reduced occurrence and severity of respiratory infection

Improves cellular **immunity**

Shown to **inhibit viral replication** (multiple viruses)

Modulates IL-6 pro-inflammatory molecules associated with cytokine storm

Precursor to glutathione, powerful antioxidant that can reduce cellular damage due to ROS

Eur Respir J. 1997 Jul;10(7):1535-41
Biochem Pharmacol. 2010 Feb 1;79(3):413-20
Medicine (Baltimore). 2018 Nov;97(45):e13087

Foods that Increase NAC and Glutathione

Allium foods	Garlic, onion, leek, shallots, scallions, spring onions, and chives
Cysteine & methionine sources	Lean meats, fish, lentils, oats, eggs, sunflower seeds

Evid Based Complement Alternat Med. 2011;2011:643269

NAC Supplementation

600-900 mg twice per day

Med Microbiol Immunol (2010) 199:291–297
DOI 10.1007/s00430-010-0155-0

ORIGINAL INVESTIGATION

Glycyrrhizin inhibits highly pathogenic H5N1 influenza A virus-induced pro-inflammatory cytokine and chemokine expression in human macrophages

Martin Michaelis · Janina Geiler · Patrizia Naczk · Patchima Sithisarn · Henry Ogbomo · Behric Altenbrandt · Anke Leutz · Hans Wilhelm Doerr · Jindrich Cinatl Jr.

Abstract Hypercytokinaemia is thought to contribute to highly pathogenic H5N1 influenza A virus disease. Glycyrrhizin is known to exert immunomodulatory and anti-inflammatory effects and therefore a candidate drug for the control of H5N1-induced pro-inflammatory gene expression. Here, the effects of an approved parenteral glycyrrhizin preparation were investigated on H5N1 virus replication, H5N1-induced pro-inflammatory responses, and H5N1-induced apoptosis in human monocyte-derived macrophages. Glycyrrhizin 100 µg/ml, a therapeutically achievable concentration, impaired H5N1-induced production of CXCL10, interleukin 6, and CCL5 and inhibited H5N1-induced apoptosis but did not interfere with H5N1 replication. Global inhibition of immune responses may result in the loss of control of virus replication by cytotoxic immune cells including natural killer cells and cytotoxic $CD8^+$ T-lymphocytes. Notably, glycyrrhizin concentrations that inhibited H5N1-induced pro-inflammatory gene expression did not affect cytolytic activity of natural killer cells. Since H5N1-induced hypercytokinaemia is considered to play an important role within H5N1 pathogenesis, glycyrrhizin may complement the arsenal of potential drugs for the treatment of H5N1 disease.

Keywords Glycyrrhizin · H5N1 · Cytokines · Monocyte-derived macrophages

Introduction

Highly pathogenic H5N1 influenza A
sidered to be potential influenza pan
[1–6]. As of March 4th 2010, 486 lab
cases of H5N1 infection have been re
resulting in 287 deaths, i.e. a morta
(http://www.who.int). The global mort
highly pathogenic pandemic 1918 H1N1 strain that caused the Spanish flu, the most severe modern influenza pandemic, was 2.5% [7]. At least for the first wave of an H5N1 pandemic, no sufficient amounts of adequate vaccines will be available [1–4, 6, 8, 9]. Therefore, antiviral therapy for influenza A viruses including highly pathogenic H5N1 virus strains remains of great importance for the first line defence against the virus [1–4, 6, 10].

The neuraminidase inhibitors oseltamivir and zanamivir as well as the adamantanes, amantadin and rimantadin, that interfere with the influenza M2 protein are licensed for the treatment of influenza [1–4, 6]. However, the use of both drug classes is limited by the emergence of resistant virus strains. In seasonal influenza strains, the majority of H3N2 viruses and a great proportion of H1N1 viruses in humans are now considered to be amantadine- and rimantadine-resistant [11–14]. Moreover, a drastic increase in osel-

Glycyrrhizin may complement the arsenal of potential drugs for the treatment of H5N1-caused disease.

antiviral activity of glycyrrhizin associated with reduced viral uptake

Med Microbiol Immunol. 2010;199(4):291-297

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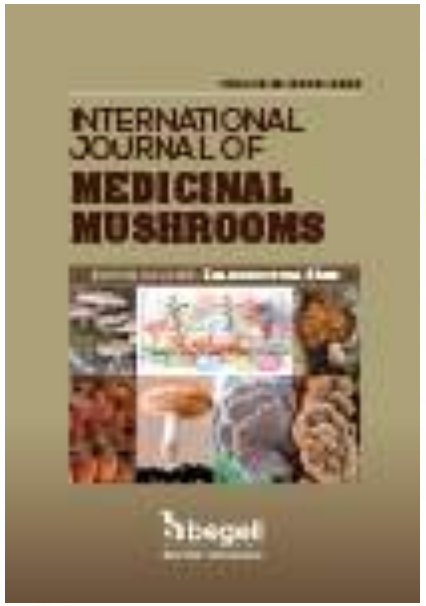
Review > Int J Med Mushrooms. 2016;18(5):375-86. doi: 10.1615/intjmedmushrooms.v18.i5.10.

Antiviral Effect of Agaricomycetes Mushrooms (Review)

Tamara V Teplyakova [1], Tatiana A Kosogova [1]

Affiliations + expand

PMID: 27649599 DOI: 10.1615/intjmedmushrooms.v18.i5.10



Abstract

This review presents data on the studied antiviral activities of Agaricomycetes mushrooms against the herpes, West Nile, influenza, human immunodeficiency, and hepatitis viruses, as well as orthopoxviruses, including the variola virus. Polysaccharides glycoproteins, terpenoids, melanins, nucleosides) exhibit ant are pathogenic in humans. Effective strains isolated from wil promising objects for the development of biotechnological d activity. The data on antitumor and antiviral activities of com species indicate the correlation of these properties. With reg Basidiomycetes may have prophylactic value in preventing c

Polysaccharides and other compounds (e.g., proteins, glycoproteins, terpenoids, melanins, nucleosides) exhibit antiviral activity against many viruses that are pathogenic in humans

Evidence that several strains are effective against H1N1 and HSV

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Randomized control trials

Supplementation with aged garlic extract improves both NK and γδ-T cell function and reduces the severity of cold and flu symptoms: A randomized, double-blind, placebo-controlled nutrition intervention

Meri P. Nantz, Cheryl A. Rowe, Catherine E. Muller, Rebecca A. Creasy, Joy M. Stanilka, Susan S. Percival*

Food Science and Human Nutrition Department, University of Florida, Box 110370, Gainesville, FL 32611, USA

ARTICLE INFO

Article history:
Received 15 September 2011
Accepted 24 November 2011

Keywords:
Aged garlic extract
Human immunity
NK cell
γδ-T cell
Colds
Flu
Garlic

SUMMARY

Background & aims: Earlier studies show that γδ-T cells. Garlic contains numerous compou shown to influence NK cell function. Our prim modify these immune cells.
Methods: A randomized, double-blind, place healthy subjects (60 per group) to determine t on immune cell proliferation and cold and flu
Results: After 45 d of consuming an encapsulat cells ($p = 0.043$, $n = 56$) were shown to prol mentation, illness diary entries showed that t not statistically different; however, the grou reduced severity as noted by a reduction in t z-test of proportions), a reduction in the num (58% fewer $p < 0.001$, z-test) where the subjects functioned sub-optimally and the number of work/school days missed due to illness (58% fewer, $p = 0.035$, z-test).
Conclusions: These results suggest that supplementation of the diet with aged garlic extract may enhance immune cell function and that this may be responsible, in part, for reduced severity of colds and flu.

Conclusions: *supplementation of the diet with aged garlic extract may enhance immune cell function and that this may be responsible, in part, for reduced severity of colds and flu*:

- NK cell proliferation (double rate)
- T-cell proliferation (8-fold)
- Glutathione and S-allyl cysteine increase
- Reduced duration, sum of symptoms, and severity (but not incidence)

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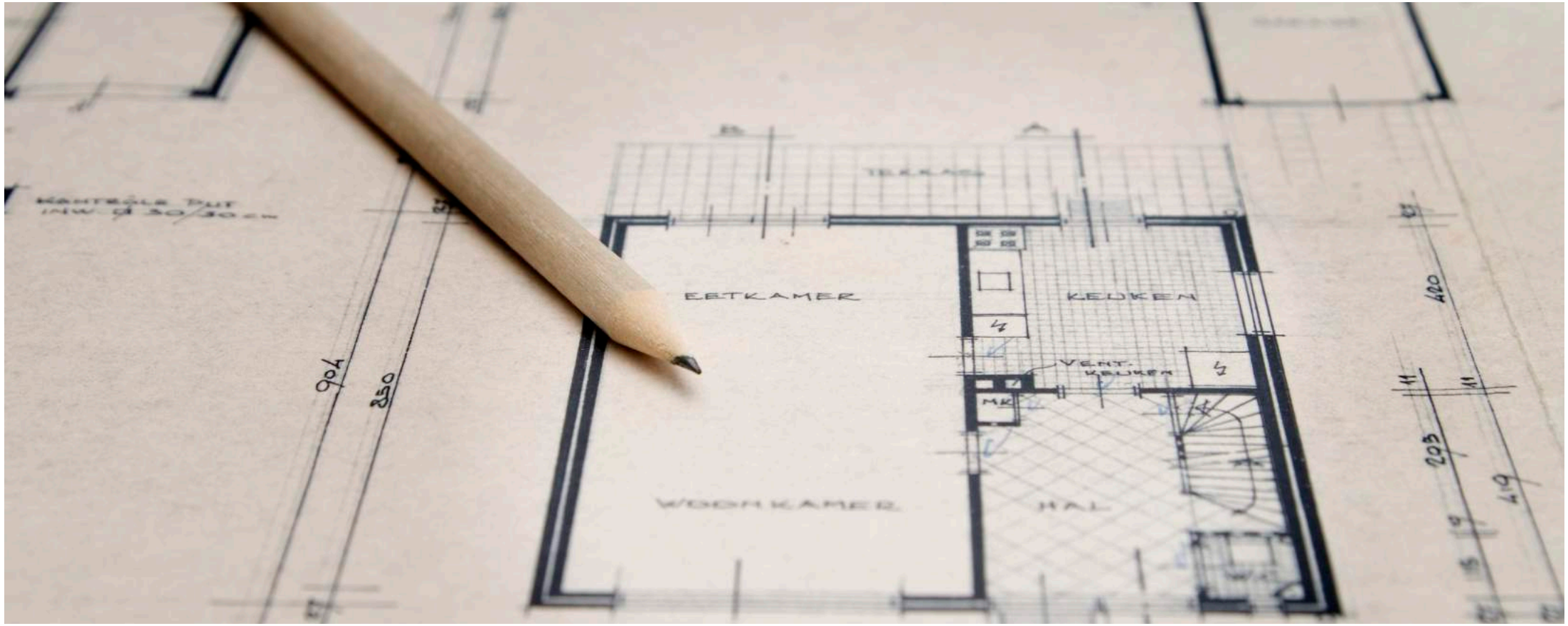
Building the Dietary and Nutraceutical Prescription



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ScienceDaily®

Your source for the latest research news

Ketogenic diet helps tame flu virus

Feed a cold, starve a fever?

Date:
November 15, 2019
Source:
Yale University
Summary:
A high-fat, low-carbohydrate diet like the Keto regimen has its fans, but influenza apparently isn't one of them. Mice fed a ketogenic diet were better able to combat the flu virus than mice fed food high in carbohydrates, according to a new study.

Mice fed a ketogenic diet were better able to combat the flu virus than mice fed food high in carbohydrates, according to a new Yale University study published Nov. 15 in the journal *Science Immunology*.

The ketogenic diet -- which for people includes meat, fish, poultry, and non-starchy vegetables -- activates a subset of T cells in the lungs not previously associated with the immune system's response to influenza, enhancing mucus production from airway cells that can effectively trap the virus, the researchers report.

They showed that mice fed a ketogenic diet and infected with the influenza virus had a higher survival rate than mice on a high-carb normal diet. Specifically, the researchers found that the ketogenic diet triggered the release of gamma delta T cells, immune system cells that produce mucus in the cell linings of the lung -- while the high-carbohydrate diet did not.

ScienceDaily. ScienceDaily, 15 November 2019. www.sciencedaily.com/releases/2019/11/191115190327.htm
Science Immunology, 2019; 4 (41): eaav2026 DOI:10.1126/sciimmunol.aav2026

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frontiers in Endocrinology

OPINION
published: 16 September 2020
doi: 10.3389/fendo.2020.574315

Mediterranean Diet and COVID-19: Hypothesizing Potential Benefits in People With Diabetes

Maria Ida Maiorino, Giuseppe Bellastella, Miriam Longo, Paola Caruso and Katherine Esposito*

Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy

Keywords: COVID-19, type 2 diabetes (T2D), mediterranean diet, inflammation, cytokines, glycemic control

INTRODUCTION

The outbreak of the Coronavirus Disease 2019
(China) and has since spread in more than 200
novel virus causing severe acute respiratory sy
comorbidities of people suffering from COVID-
disease, and hypertension, all of which are assoc

People with diabetes are at increased risk of s
SARS-CoV, H1N1 influenza, and Middle East R
of diabetes in individuals with COVID-19 has b
30%, depending on the location of the study, po
of illness, and method of testing (2). Moreove
of severity of the SARS-CoV-2, as the risk of fat
in individuals with diabetes than in those without (3). Given the high transmission rate of SARS-CoV-2 and the global prevalence of diabetes, which affects nearly half a billion people worldwide, the coexistence of both COVID-19 and diabetes should be considered alarming, as it represents the combination of two pandemics.

OPEN ACCESS

Edited by:
Alexandra Kautzky-Willer,
Medical University of Vienna, Austria

Reviewed by:
Burkhard J. Göke,
Medical School Hamburg, Germany

In two RCTs of people with obesity and metabolic syndrome, the consumption of Mediterranean diet for 2 years was associated with a significant reduction of inflammatory markers, including CRP, IL-6, IL-7, and IL-18, as compared with a prudent diet. The MEditerranean DIet and Type 2 diAbetes (MÈDITA) study, provides further evidence of the anti-inflammatory and immunomodulatory effect of Mediterranean dietary pattern in the context of diabetes.

frontiers in Endocrinology

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Mediterranean Diet and COVID-19: Hypothesizing Potential Benefits in People With Diabetes

Maria Ida Maiorino, Giuseppe Bellastella, Miriam Longo, Paola Caruso and Katherine Esposito*

The mechanisms by which Mediterranean diet produces its favorable effects in type 2 diabetes may depend mostly on the abundance of anti-inflammatory nutrients (PUFA, fiber, vitamins, minerals, antioxidants, and polyphenols), associated with the lower intake of pro-inflammatory nutrients (refined sugars and starches, trans fatty acids, high-density foods).

Anti-inflammatory effects via:

- Specialized pro-resolving mediators
- α-linolenic acid
- Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
- Increased dietary fiber intake (associated with reduced inflammatory markers hs-CRP, IL-6, & TNF-α) and favorable modifications in gut microbiota
- Increased intake of key vitamins (Vit D via ACE2 viral entry; Vit C & E antioxidant)
- Polyphenols seem to interact with transcription factors, including NF-kB and Nrf-2, exerting anti-inflammatory and antioxidant effects

Dietary recommendations

Dietary Considerations

Plant-based (80/20)

- Macronutrient balance
- Micronutrient-dense
- Phytonutrient-rich

Mediterranean diet

- Little data on direct impact on viral/bacterial infection
- Solid data on impact on metabolic aspects that support immune balance

Ketogenic

- More challenging to sustain than MedD
- Some utility in viral infection
- Like MedD, benefits might be more connected to metabolic impact though some data support inflammatory response (T-cell)

Fasting

- Intermittent Fasting, time restricted eating,
- Caloric restriction and Fast Mimicking Diet (FMD)
- Fast/modified fast (water fats, juice fast)

Published in final edited form as:
Mol Cell Endocrinol. 2017 November 05; 455: 4–12. doi:10.1016/j.mce.2017.01.042.

Nutrition and fasting mimicking diets in the prevention and treatment of autoimmune diseases and immunosenescence

In Young Choi[a,b], **Changhan Lee**[a], and **Valter D. Longo**[a,c,d,e,*]

Abstract

Complex and coordinated signals are necessary to initiate and sustain the activation, proliferation, and differentiation of lymphocytes. These signals, which are known to determine T-cell fate and function, also depend on the metabolic state of the organism. Recent studies indicate that both the type and levels of nutrients can influence the generation, survival and function of lymphocytes and therefore can affect several autoimmune diseases. Here, we review the dysregulation of lymphocytes during autoimmunity and aging, the mechanisms associated with loss of immune function, and how fasting mimicking diets and other dietary interventions affect autoimmunity and immunosenescence.

Keywords

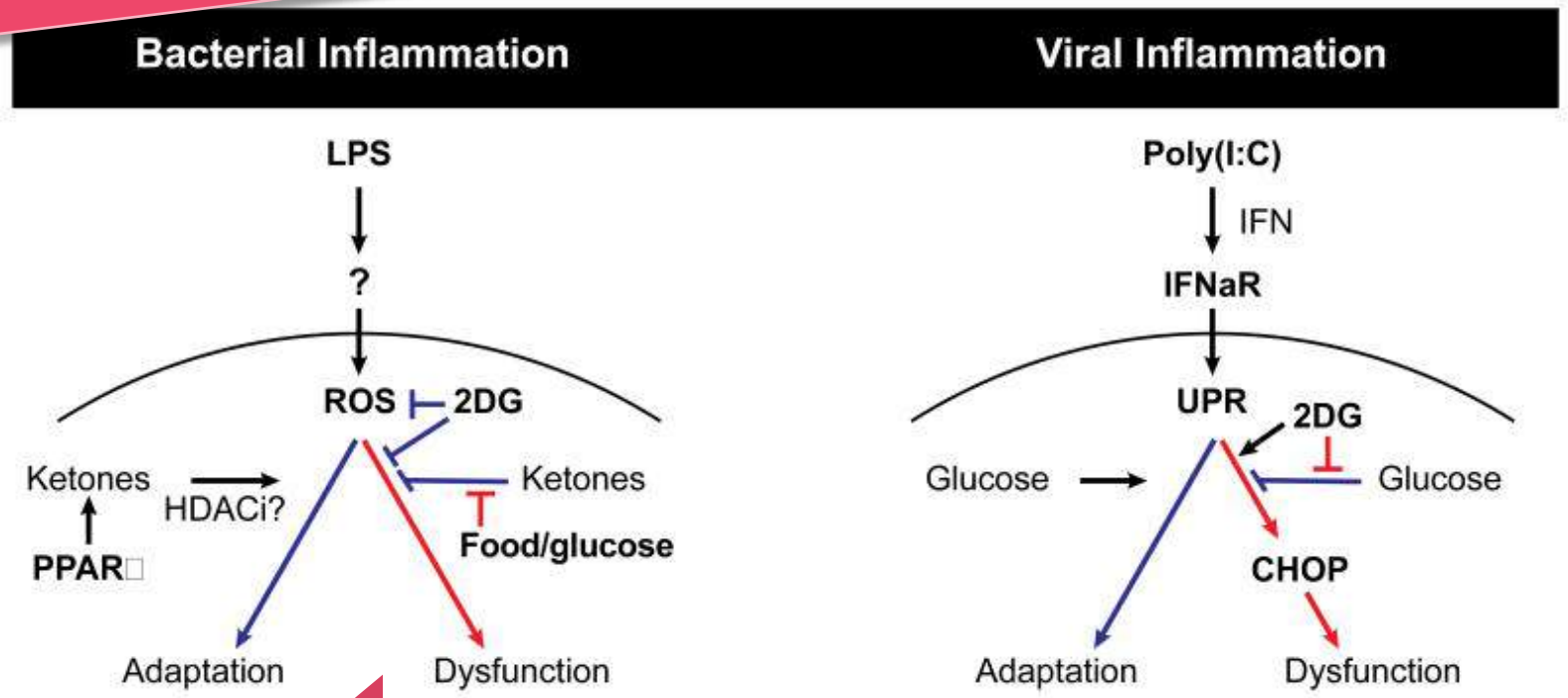
Immunosenescence; Autoimmune diseases;

1. Introduction

Aging is associated with a progre
referred to as immunosenescence
immunosenescence, including incr
diseases, reduced response to vaccination, and chronic inflammation (Franceschi and Campisi, 2014; Franceschi et al., 2000). In general, men experience a stronger age-dependent alteration of immune function than women (Yan et al., 2010).

…periodic IF/FMD combines a period of severe restriction sufficiently long to promote the **death of a significant portion of damaged cells** with a period of high nourishment re-feeding able to promote the opposite effect on growth and other factors leading to **multi-system regeneration**

Feed a cold, starve a fever



Inhibition of glucose utilization during bacterial inflammation protective

Inhibition of glucose utilization in viral inflammation leads to tissue dysfunction and death

Cell. 2016;166(6):1512-1525.e12

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What's the role of fasting in immunity?

Improved Nrf2 response (ARE activation and antioxidant response)

Improved resilience for viral infection

Does not seem to impact susceptibility to viral infection

May increase risk for bacterial susceptibility (reduced availability of micronutrients)

Should be avoided for bacterial infection

General Dietary Summary

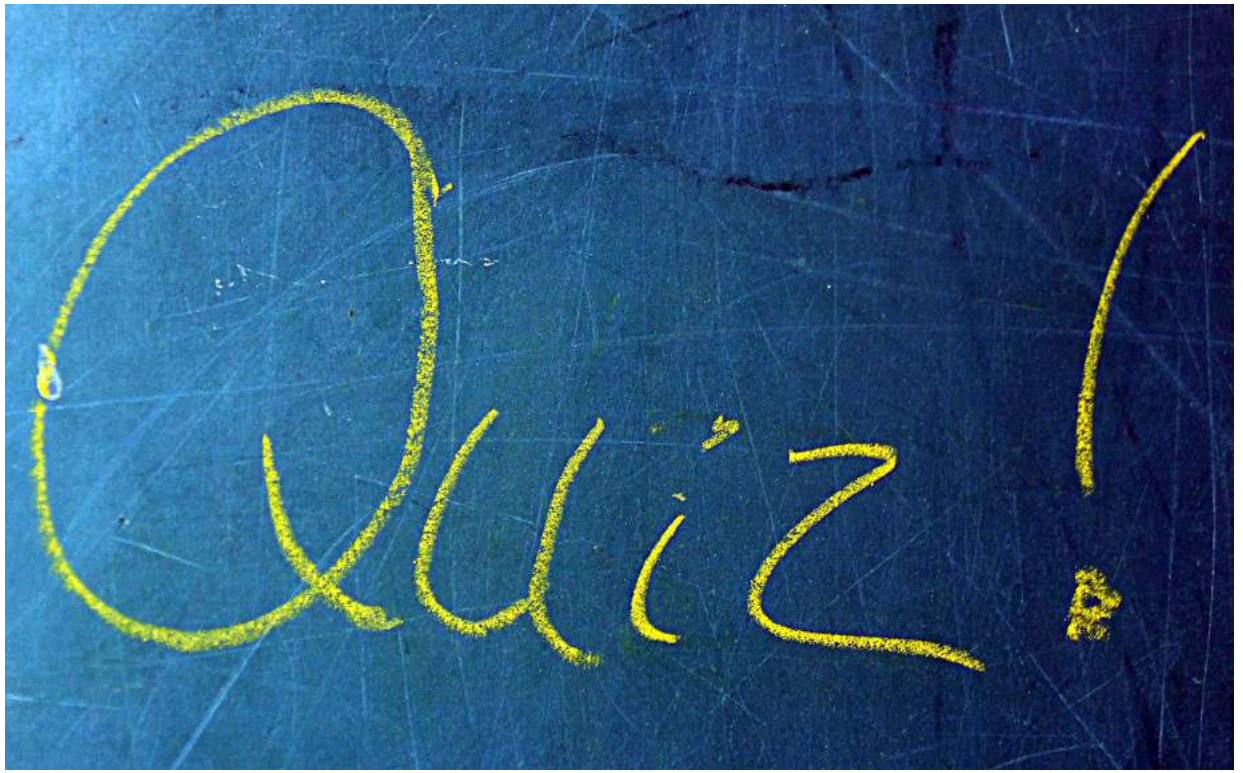
Increase/Emphasize

- Plant-based dietary diversity, Fiber – dense foods
- Antiinflammatory (PUFA) fats
- High nutrient density sources of protein (red meat, poultry, fish, and plant-based protein)
- Phytonutrient sources including mushrooms, EGCG, curcumin, rosemary.
- Alliums and cruciferous foods
- Maintain adequate hydration: ½ the person's body weight (in pounds) in fluid ounces

Remove/Avoid

- Avoid inflammatory foods: processed foods, starchy foods, high glycemic foods, hydrogenated oils, and juices/soda
- Avoid known allergens or food triggers that might increase allergenic response
- Reduce toxic burden (organic, avoid heavy metals, pollution, plastics, etc…)

Let’s take a survey



Considerations

Meet your patient were they're at …

- Level of nutrition literacy
- Access (geographic, financial)
- Skills
- Time limitations
- Cultural considerations

Good, Better, Best
(don’t make assumptions)

- Crowd out junk
- Mediterranean Diet
- Paleo
- Keto

Considerations

Meet your patient were they're at …

- Level of nutrition literacy
- Access (geographic, financial)
- Skills
- Time limitations
- Cultural considerations

Refer to a nutritionist or health coach!!

- Nutritionist can tailor a plan to the patient's needs
- Health coaches = transformation guides

Therapeutic Foods to Include

Healthy fats

- Extra-virgin olive oil (EVOO), nuts and seeds
- Omega-3 fat sources from food (and supplement sources 2 to 4 grams per day)

Antioxidants

- Alliums (especially garlic) & cruciferous vegetables
- Green tea (EGCG), resveratrol, carotenoids

Fiber sources

- Non-starchy vegetables, colorful root vegetables
- Whole Grains and legumes (limit processing)
- Traditionally fermented foods

Focus on color "eat the rainbow"

- Phytonutrients: Organic, colorful mix of low glycemic veggies & fruit
- Mushrooms
- Cinnamon, turmeric, ginger, rosemary (and others)

Chicken Soup Cure May Not be a Myth

Chicken soup may provide relief from the symptoms of the cold season through neutrophilic action. There are an estimated 20 to 50 million influenza virus infections annually in the United States, resulting in 24 million patient visits, 300,000 hospitalizations, and 20,000 to 50,000 deaths.[1] The synergistic properties of chicken soup may decrease the inflammatory response associated with viral illnesses.

The Neutrophil Response

The body responds to cold symptoms in the form of a hypersensitivity reaction.[2] During this reaction, the human body experiences an inflammatory response that Cohnheim describes as having three characteristics: 1) blood vessel dilation, which increases blood pors raises the temperature of the respiratory passages and loosens thickened secretions.[6]

An in vitro project initiated in 1998 and later published in October 2000 tested the effectiveness of market brand soup products for the ability to inhibit neutrophilic activity.[3] The project found that soup significantly inhibited neutrophil migration with activity responsive in the solution or liquid part of the soup mixture.[3]

Hot Water or Hot Soup?

Nasal airflow resistance was measured in 15 healthy subjects before drinking hot water, chicken soup, and cold water, and then in 5- and 30-minute intervals.[7]

The researchers concluded that drinking hot fluids helped to increase to inhibit neutrophils during cold symptoms. "Grandma's recipe" contained most of the same ingredients as traditional recipes including spices such as parsley, sage, thyme, salt and pepper.

Thirteen of the 14 brands inhibited neutrophil movement less potently than "Grandma's recipe." One brand, Campbell's Ramen Noodles, Chicken Flavor, had a greater amount of chemotaxis than the control recipe. In this project, tap water was heated and accounted for a higher rating due to its vaporous quality.

Patient Management

More research is needed to find out which ingredients are most effective. Focusing on our body defenses through chemotaxic activity may minimize medications.

Nurse Pract. 2003 Jun;28(6):16

A rhinoviral cold is characterized by a neutrophilic inflammatory reaction. Mediation of cytokines and mediators play a crucial role in rhinovirus infection.

Bone broth's medicinal properties by modulating the inflammatory response associated with viral illnesses.

Benefit is especially synergistic when combined with traditional ingredients like celery, onions, garlic, carrots, parsley, mushrooms, parsnips and other herbs known for their added medicinal and antioxidant properties.

Furthermore, chicken soup provides additional nutritional support, fluid balance and hydration. Therefore, it might be an effective tool for patient care management of seasonal cold & flu.

Nurse Pract. 2003 Jun;28(6):16
Acta Otorhinolaryngol Belg. 2000;54(3):397-401

Foods to Avoid or Minimize

Sources of toxins

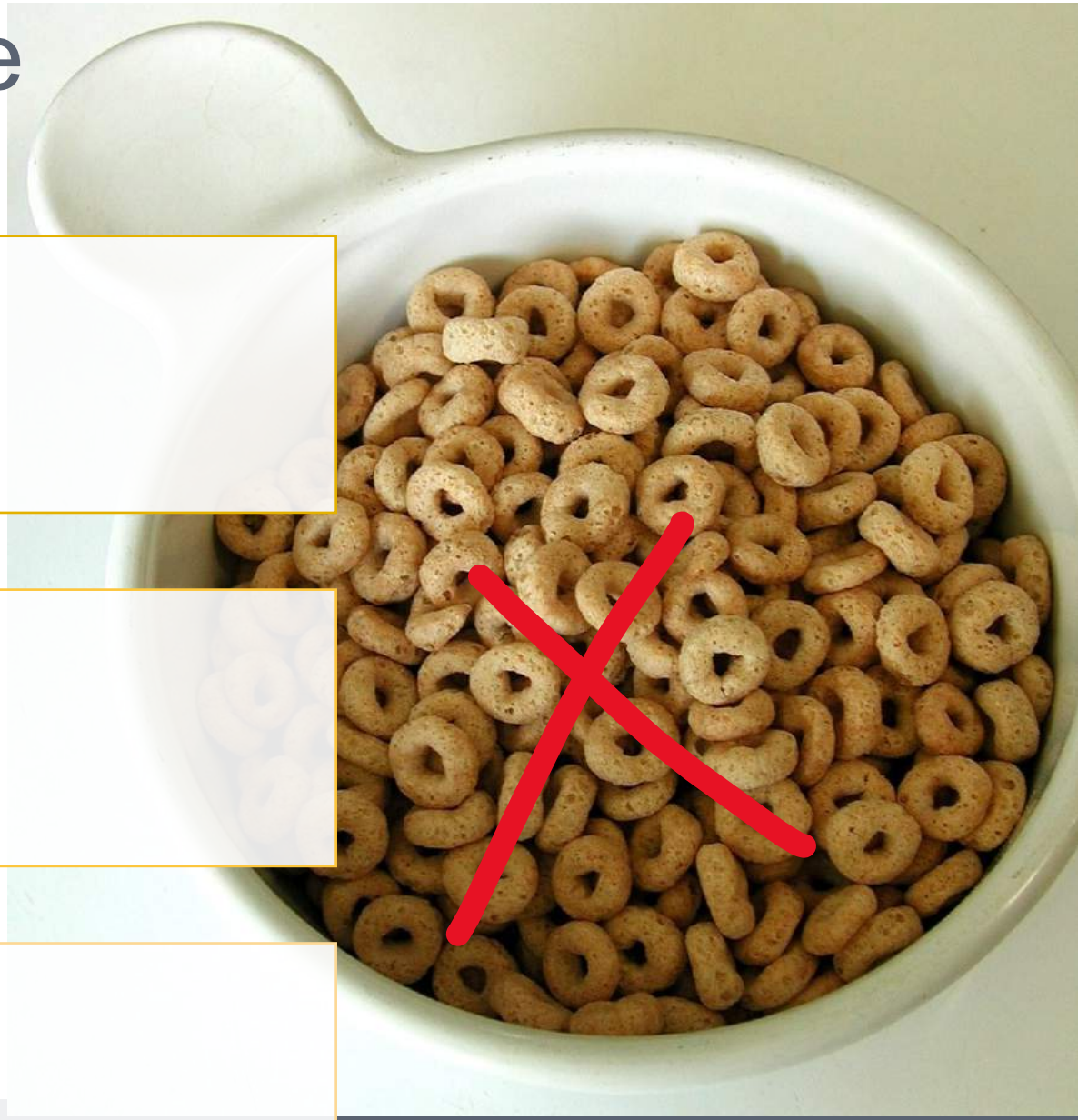
- Pesticide exposed foods
- Conventionally raised animal products
- Food or drink in plastic containers

Processed foods & refined carbohydrates

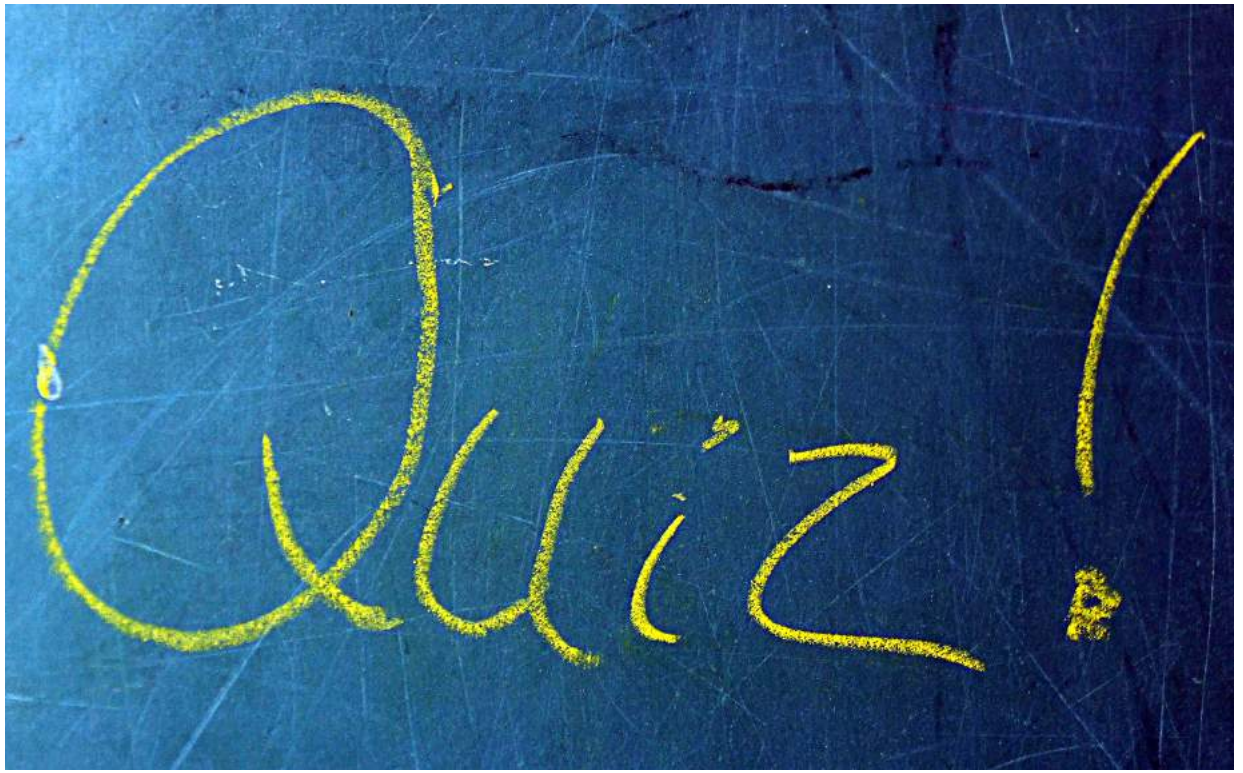
- Soda, fruit juices, sucrose, and fructose
- Artificial sweeteners
- Fast foods

AGEs

- Over-cooking foods
- Fried foods



Let’s test our foundational knowledge



Role of supplements

Nutraceuticals: The Workhorses

- Zinc
- Vitamin A and beta-carotene
- Vitamin C
- Vitamin D (with K)
- Vitamin E (and other antioxidants selenium, ALA, etc)
- Fish oil
- Pre- and probiotics

Nutraceuticals: Dosing

Zinc	• 15-30mg/day; up to 60mg in COVID • Caution on copper ratio in long-term supplementation • Zinc acetate, citrate, picolinate, or glycinate (lozenge for COVID)
Vitamin A and beta-carotene	• Can be as high as 20,000 IU in early onset of infection
Vitamin C	• 500-2000mg/day • I like liposomal or buffered
Vitamin D (with K)	• Caps or drops dosing 5000 IU/day of Vit D (with K2 unless there's a clear contraindication) • Adjust dose based on laboratory evaluation
Vitamin E	• 200-400 mg/day • Vit E within a broad antioxidant formula
Fish oil	• 1-2g/day unless there's a clear cardiometabolic indication • 4g/day in combination with antioxidants to prevent lipid oxidation
Pre- and probiotics	• Food sources of fiber preferred, supplementing with fiber sources like Arabigalactan, pectin, guar gum, rice bran etc… • Probiotic with a broad profile (caution for tolerance those with dysbiosis might not tolerate these)

Nutrients/Compounds with antimicrobial/antiviral properties

- Zinc
- Citrus
- Green tea
- Berries
- Ginger
- Garlic
- Mushrooms
- Raw honey
- Rosemary
- Tumeric
- Quercetin

Nutraceuticals: Additional Considerations

GI, Mitochondrial & detoxification support
*Specialized proresolving mediators (SPMs)
*Palmitoylethanolamide PEA
*Melatonin
NAC and glutathione
Quercitin and bioflavonoids
*Mushrooms (beta-glucans)
Garlic (allicin)
*Green tea extract (EGCG)
Ginger *(Zingiber officinale)*
*Curcumin
*Resveratrol
*Astragalus
Echinacea
*Elderberry

*some additional research shows benefits in COVID in particular

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Useful dosing guidelines for COVID

Palmitoylethanolamide PEA	• 300 mg po bid to prevent infection, • 600 mg po tid x two weeks to treat infection
Melatonin	• 5-20 mg qd
NAC and glutathione	• NAC 600-900 mg po bid
Quercitin and citrus bioflavonoids	• Regular: 1 gm po bid; phytosome 500 mg bid
Mushrooms (beta-glucans)	• Beta-glucans 250-500 mg daily • Shiitake (Lentinula edodes), Lion's Mane (Hericium erinaceus), Maitake (Grifola frondosa), Reishi (Ganoderma lucidum)
Green tea extract (EGCG)	• 225 mg po qd (equivillent to 4 cups/day)
Curcumin	• 500-1,000 mg po bid (of absorption-enhanced curcumin)
Resveratrol	• 100-150 mg po qd • Modulation of NLRP3 inflammasome activation
Astragalus	• Dosage range varies between 1-20 grams daily • immunoactive polysaccharides
Elderberry	• 500 mg po qd (of USP standard of 17% anthocyanosides) • *Favorably modulate cellular defense and repair mechanisms* *Favorably modulate viral-induced pathological cellular processes*

https://www.ifm.org/news-insights/functional-medicine-approach-covid-19-additional-research-nutraceuticals-botanicals/
https://www.ifm.org/news-insights/the-functional-medicine-approach-to-covid-19-virus-specific-nutraceutical-and-botanical-agents/

Other considerations

Detoxification Support

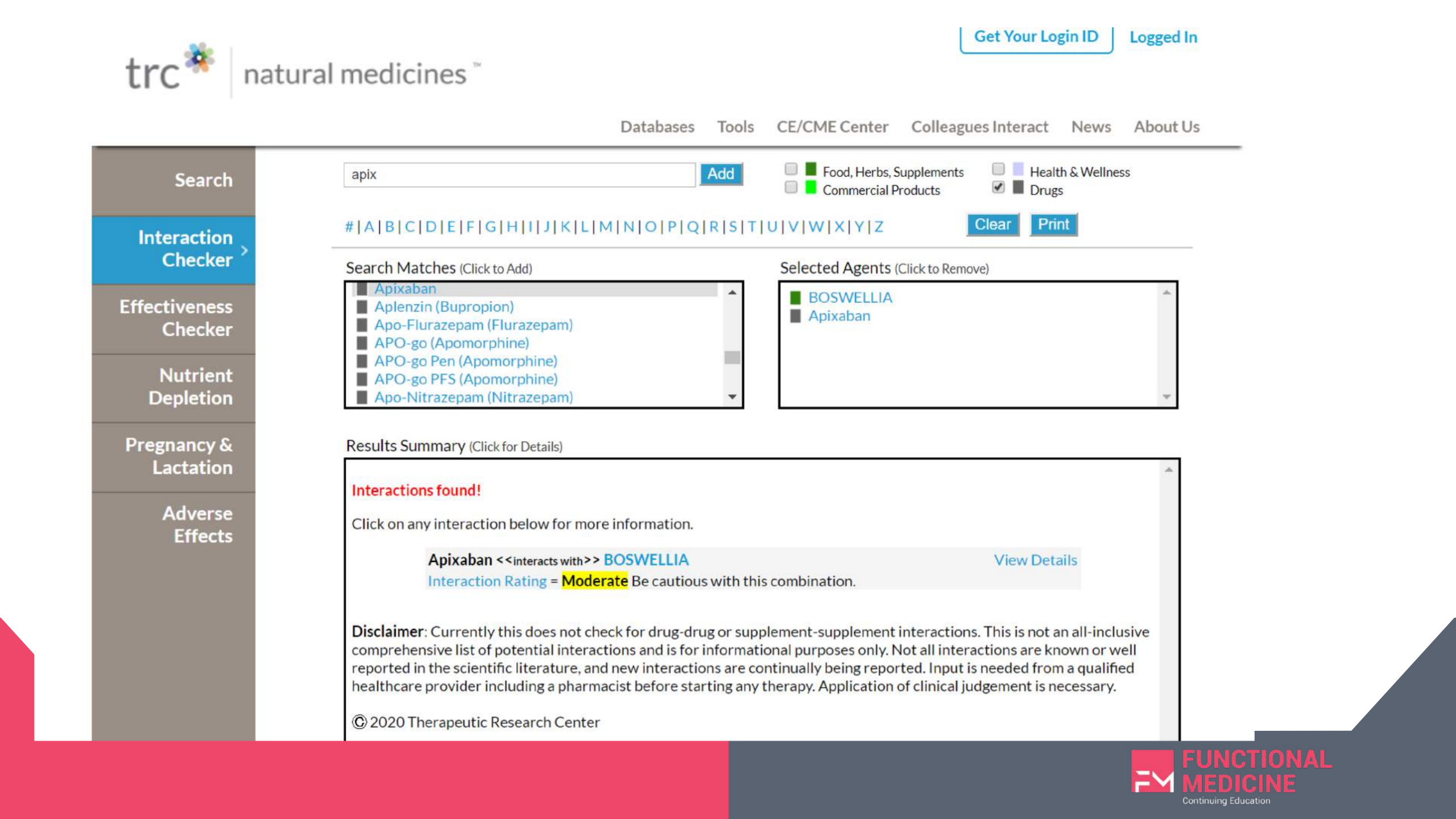
- B-complex (methylated)
- NAC
- Glutathione and precursors

GI support

- 5R protocol
- Probiotics
- Prebiotics

Hormone balance

- Sex hormones
- Cortisol
- Insulin (berberine)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Interaction Checker
Effectiveness Checker
Nutrient Depletion
Pregnancy & Lactation
Adverse Effects
apix
Add
Food, Herbs, Supplements
Commercial Products
Health & Wellness
Drugs
| A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z
Clear
Print
Search Matches (Click to Add)
Apixaban
Aplenzin (Bupropion)
Apo-Flurazepam (Flurazepam)
APO-go (Apomorphine)
APO-go Pen (Apomorphine)
APO-go PFS (Apomorphine)
Apo-Nitrazepam (Nitrazepam)
Selected Agents (Click to Remove)
BOSWELLIA
Apixaban
Results Summary (Click for Details)
Interactions found!
Click on any interaction below for more information.
Apixaban <<interacts with>> BOSWELLIA
View Details
Interaction Rating = Moderate Be cautious with this combination.
Disclaimer: Currently this does not check for drug-drug or supplement-supplement interactions. This is not an all-inclusive comprehensive list of potential interactions and is for informational purposes only. Not all interactions are known or well reported in the scientific literature, and new interactions are continually being reported. Input is needed from a qualified healthcare provider including a pharmacist before starting any therapy. Application of clinical judgement is necessary.
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FUNCTIONAL MEDICINE
Continuing Education

The Nutrition & Lifestyle Prescription

THE INSTITUTE FOR FUNCTIONAL MEDICINE

Functional Medicine Prescription

Patient Name _____ Date of Birth _____

Functional Nutrition Prescription

Functional Nutrition
- ☐ Phytonutrient Spectrum
- ☐ Core Food Plan (CFP)
- ☐ CFP, modified: _____

First Step Interventions
- ☐ Elimination Diet
- ☐ Food Reintroduction
- ☐ Cardiometabolic Food Plan

Advanced Interventions
- ☐ GI Specific Food Plans
- ☐ Detox Food Plan
- ☐ Mito Food Plan

Personal Dietary Recommendations

Macronutrient Distribution: ☐ 45/25/30 ☐ 40/30/30 ☐ Mild/Strict Keto ☐ Intermittent Fasting _____ days/wk

Target Calories: ☐ 600 ☐ 1000–1200 ☐ 1200–1400 ☐ 1400–1800 ☐ 1800–2200 ☐ 2200–2500

_____

_____

Lifestyle Prescription

☐ **Sleep:** _____

☐ **Exercise:** Risk Assessment: ☐ Low Risk ☐ Medium Risk ☐ High Risk

Clearance: ☐ Yes ☐ No _____

Exercise Prescription:	Cardio/Aerobic	Strength/Resistance	Flexibility/Stretching	Balance
F – Frequency times per week				
I – Intensity (e.g., low, moderate, vigorous)				
T - Time/duration minutes each day				
T – Type (e.g., walking, jogging, swimming)				

☐ **Stress management:** _____

Supplements/Medications Prescription

Supplement/ Medication	On rising	Breakfast	Mid-morning	Lunch	Mid-afternoon	Dinner	Mid-evening	Before bed

Additional Comments _____

_____

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Summary

Dietary interventions to support immunity:

- Phytonutrient diversity, low-glycemic, healthy fats
- Support detoxification, mitochondrial function, and GI health
- Avoid potential inflammatory triggers

Determine when to incorporate nutrient supplementation alongside dietary approaches.

- Include foundational micronutrient support for immune balance
- Don’t shy away from herbals, but use best clinical judgement when dealing with polypharmacy

lara zakaria

RPh MS CNS | @FOODIEFARMACIST

Questions?

Visit http://LaraZakaria.com

Email Hello@LaraZakaria.com

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