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GLP-1 Agonists and Alternatives: What You Need to Know

with Michael T. Murray, N.D.

"Let your food be your medicine and your medicine be your food."

Hippocrates

GLP-1 Drugs: What You Need to Know

Agenda:

- What is GLP-1 and what are GLP-1 Agonists?
- Concerns, Side Effects, and Benefits
- Natural Alternatives to GLP-1 Agonists
  - Overview
  - PGX®
  - Berberine
  - Akkermansia muciniphila
  - Oleoylethanolamide (OEA)
  - Morosil®
- For More Information

What is GLP-1

- Hormone secreted by L-cells in the small intestine and colon that:
  - Improves insulin action and blood sugar control
  - Promotes satiety, leading to reduction of food intake
  - Regulates the rate of gastric emptying, thereby reducing after-meal glucose levels

What are GLP-1 Agonists

- Drugs that mimic the action of GLP-1
  - Semaglutide (Ozempic and Wegovy)
  - Tirzepatide (Mounjaro and Zepbound)
- GLP-1 agonists help 60% of patients achieve a 20% reduction in body weight. But….
  - Side effects
  - Safety issues
  - Weight regain if they stop taking

What are My Concerns

- The duration of action is different than the endogenous GLP-1.
- The use of these drugs create a dependence.
- GLP-1 agonists disproportionately promote loss of muscle mass.
- Weight loss without positive changes in diet and lifestyle may not provide long-term benefit.

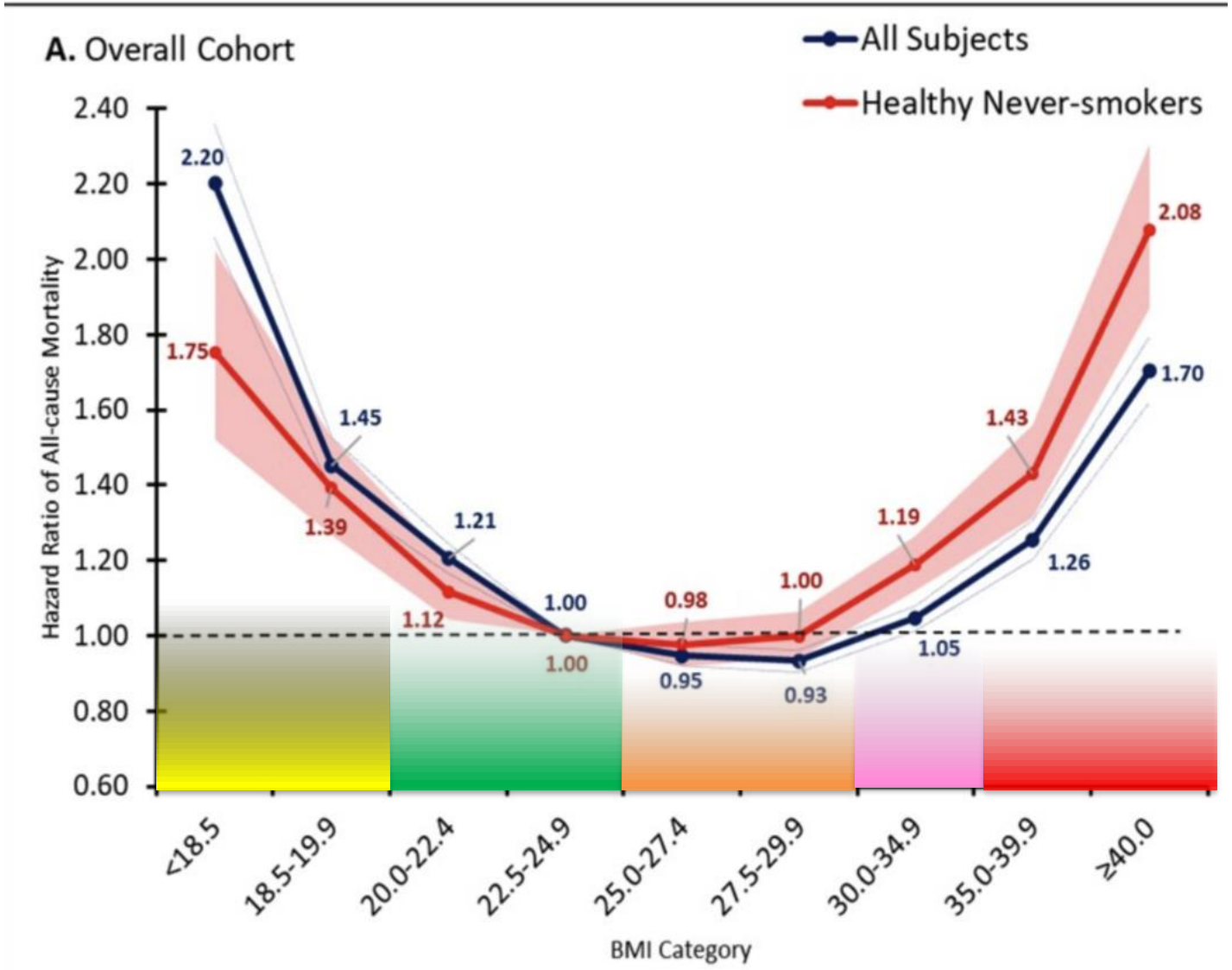
Some Additional Considerations

- Obesity and health is a complex issue
- Obesity increases morbidity, but being up to 50 pounds overweight only shortens life expectancy by 3 years
- Does losing weight improve how people look and feel
- Do the benefits of GLP-1 agonists outweigh potential risks
- Cost?

Obesity increases the risk of many health issues

Obesity and Life Expectancy

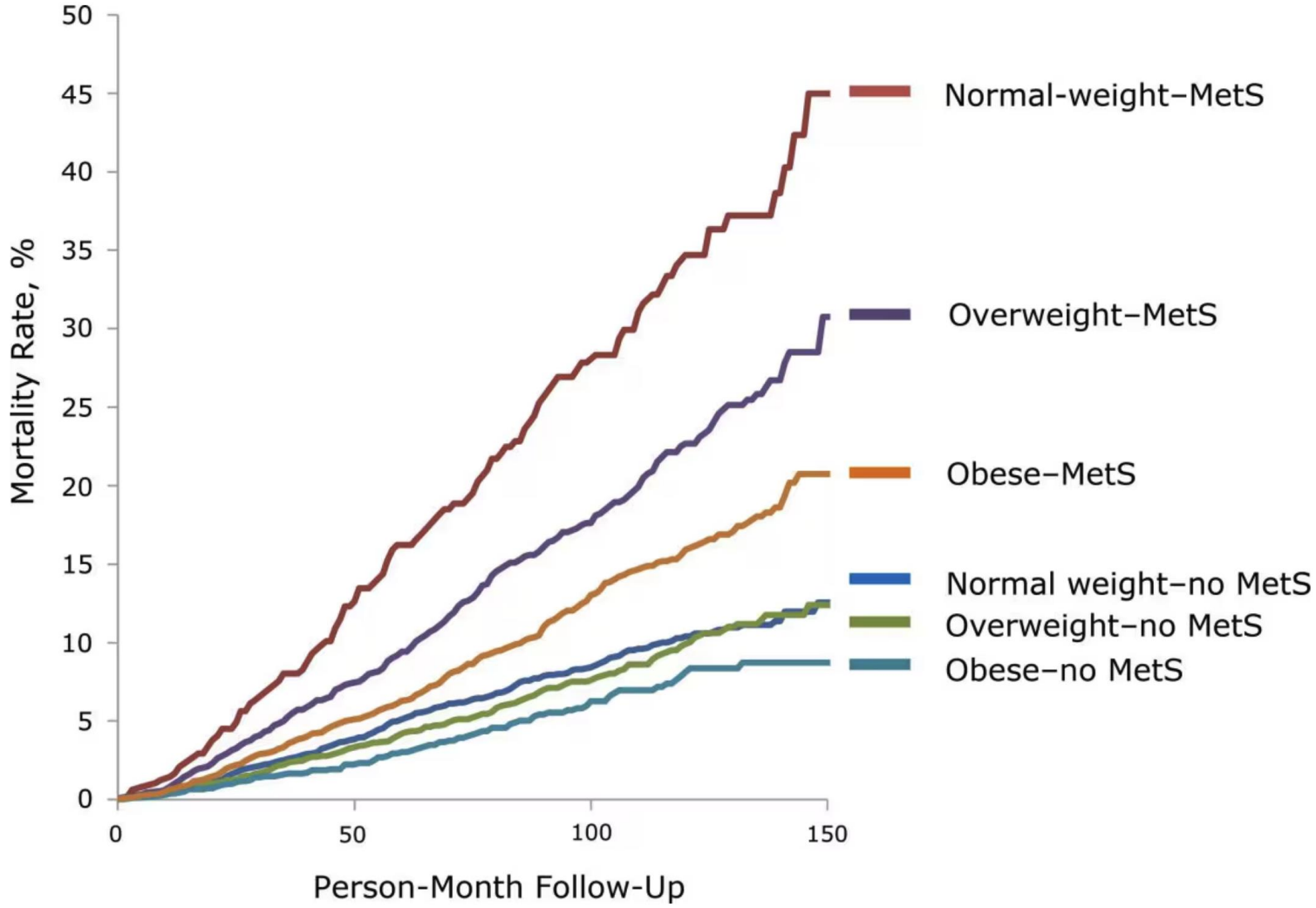
Mortality risk based upon Body Mass Index in U.S.



Underweight
Normal
Overweight
Obese
Very Obese

BMI and Mortality in MetS

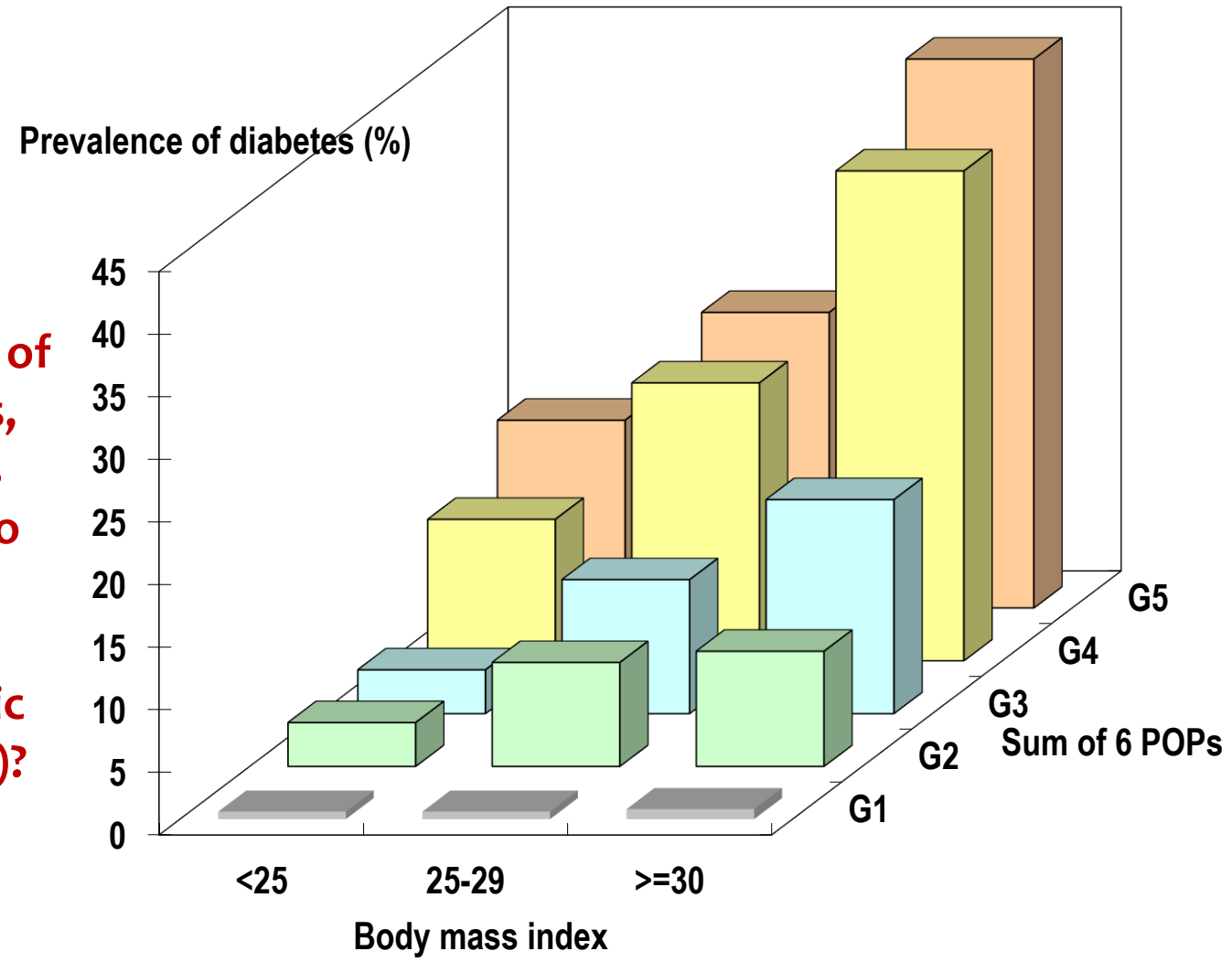
Mortality risk based upon Body Mass Index in Metabolic Syndrome



Prev Chronic Dis 2020;17:200020.

POPs and Diabetes

Are the epidemics of obesity, diabetes, and Alzheimer's disease related to the increased exposure of persistent organic pollutants (POPs)?



Lee DH, et al. Diabetes Care 2006

Who Should Consider GLP-1 Agonists?

The Best Candidates:

- Those with a BMI > 35
- Those with obesity-related morbidity, especially heart disease and diabetes
- Those that incorporate necessary lifestyle and dietary strategies that support health
- Those that understand the risks and benefits

Who Should Consider Natural Alternatives?

The Best Candidates:

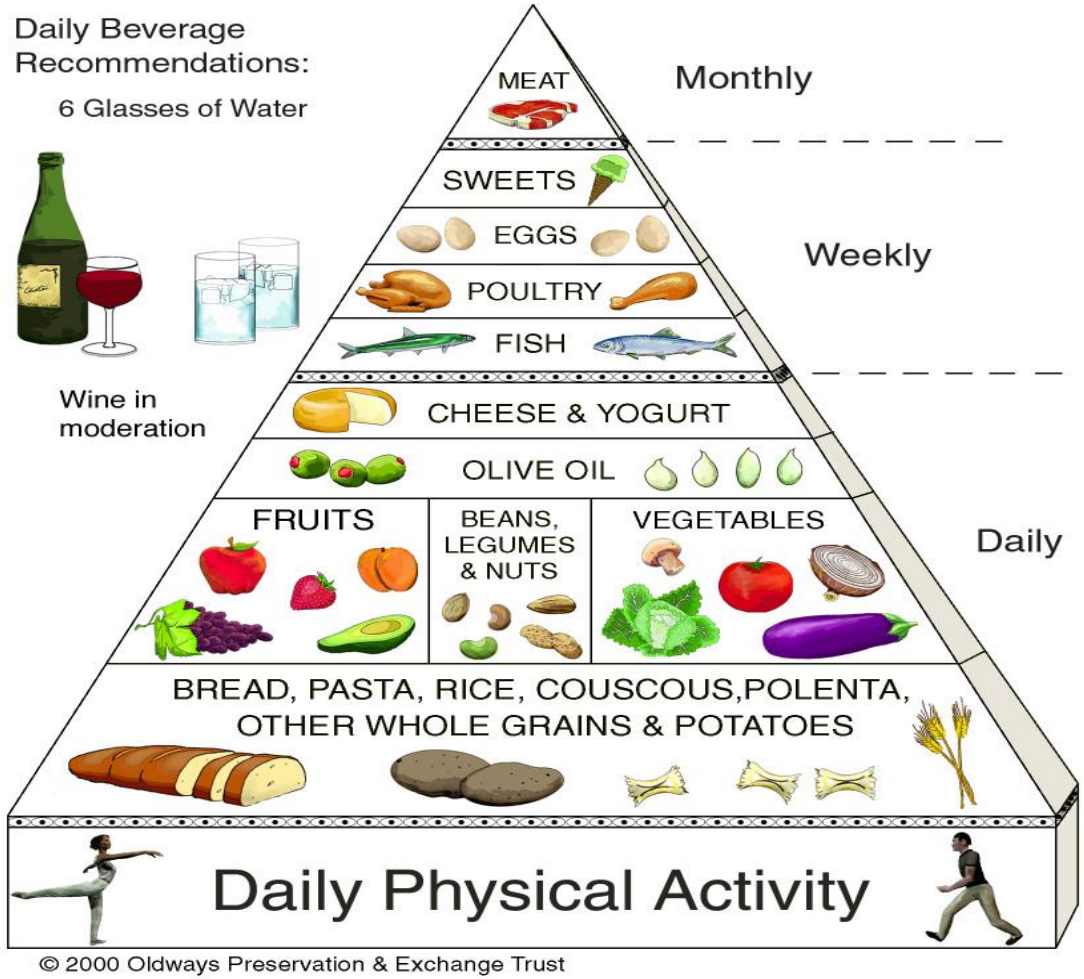
- Those who cannot afford or do not want to use a GLP-1 agonist
- Those without significant obesity-related morbidity, i.e., healthy individuals
- Those that can easily achieve weight loss goals without use of GLP-1 agonists.
- Those highly committed to incorporating necessary lifestyle and dietary strategies that support health

5 Keys to Lose Weight Naturally

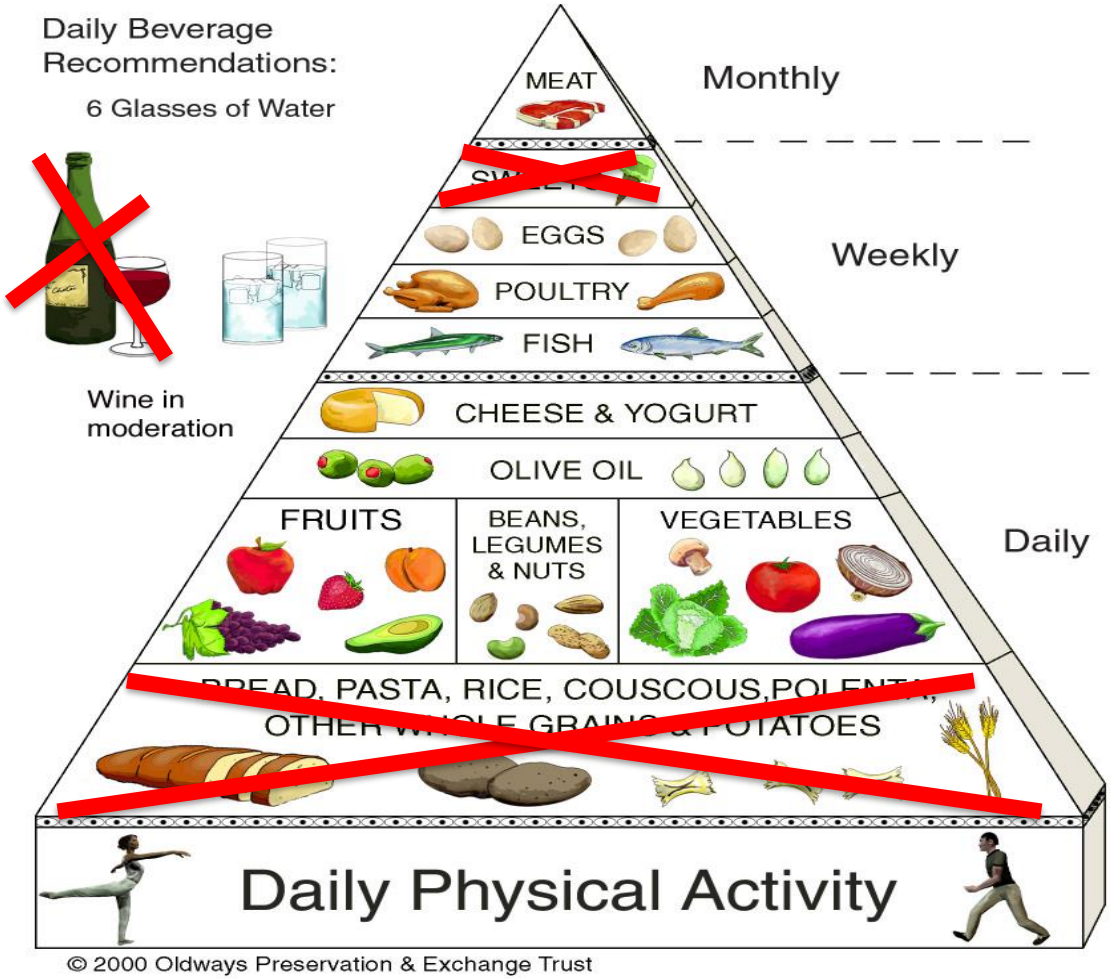
- Focus on quality nutrition, not starvation
- Move more and build muscle
  - Activate non-exercise activity thermogenesis
- Use “modified” intermittent fasting with an 8-hour feeding window and portion control
- Activate GLP-1 and **AMPk** with natural metabolic aids

Eat a ”Rainbow Diet” and Take Advantage of Superfood Powders

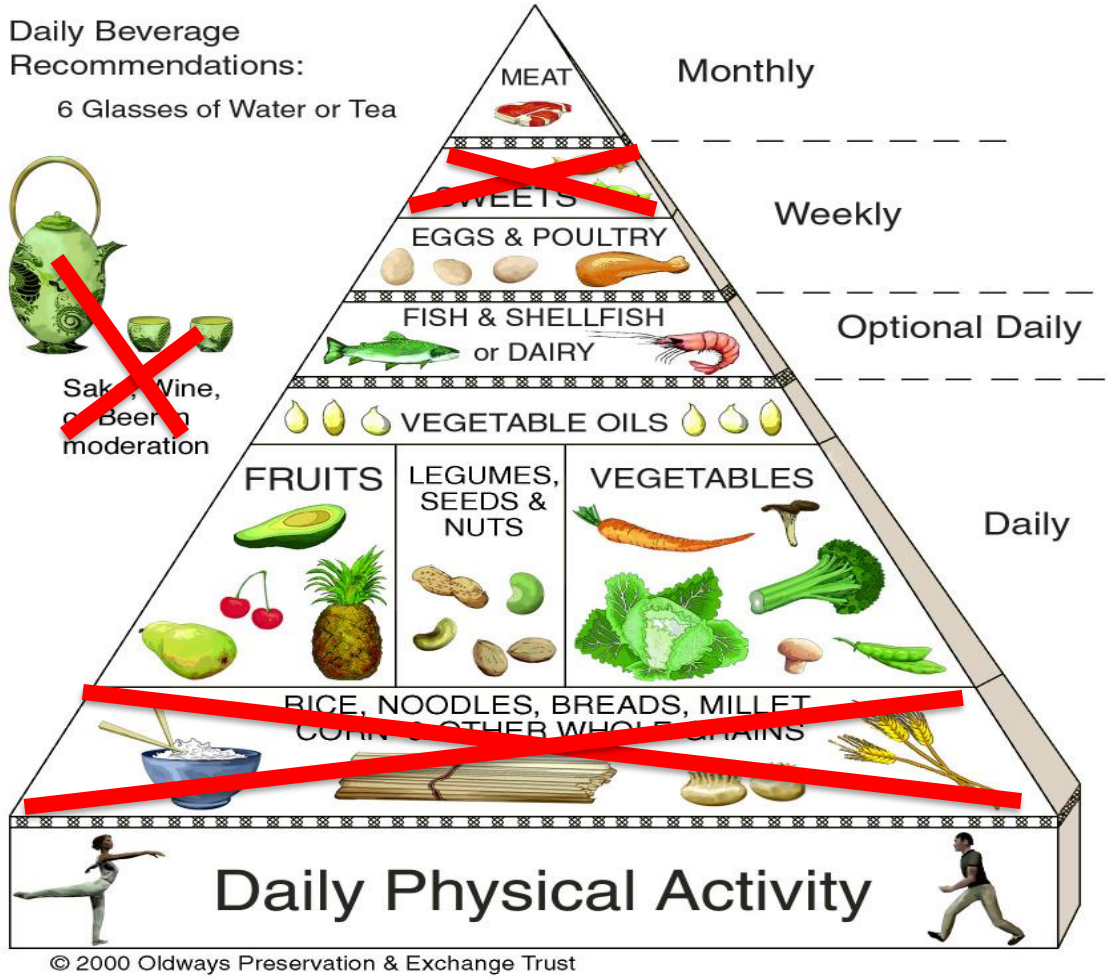
The Traditional Healthy Mediterranean Diet Pyramid



The Traditional Healthy Mediterranean Diet Pyramid



The Traditional Healthy Asian Diet Pyramid



Top 5 Natural GLP-1 Alternatives

- PGX®
- Berberine
- *Akkermansia muciniphila*
- Oleoylethanolamide (OEA)
- Morosil®

AMP-activated protein kinase: A Target for Modern Humans

Consequences of Low AMPk Activity

- Decreased numbers and function of mitochondria
- Increased abdominal fat (visceral obesity)
- Increased systemic inflammation
- Insulin resistance and elevated blood sugar levels
- Elevated blood lipids (cholesterol and triglycerides)
- Cellular degeneration (e.g., neurodenegeration)

Activators of AMPk

Intense exercise
Calorie restriction/Intermittent fasting
Thyroid hormone
Adiponectin
Highly viscous dietary fiber (PGX)
Good oils
- **Olive oil (and polyphenols)**
- **EPA+DHA**
- **MCTs**

Mitochondrial enhancers
- Alpha-lipoic acid
- Creatine
- Carnitine
- Coenzyme Q10

Various flavonoids/ polyphenols
- **Anthocyanins**
- **Curcumin**
- Green tea (EGCG)
- Genistein
- PCOs
- Chlorogenic acid (green coffee extract)

Numerous botanicals
- **Berberine**
- Mulberry leaf
- Cinnamon

Allulose

Avoid Inhibitors of AMPk
- **High fat diet**
- **Caloric excess**
- **Sedentary lifestyle**
- **Aging**

Allulose – The Holy Grail of Sweeteners

- Naturally occurring sugar that is 80% as sweet but has only 1/10th the calorie level of sucrose or fructose.
- Allulose is absorbed from the gastrointestinal tract, so it does not cause the gas and bloating that sugar alcohols like xylitol, erythritol, etc.
- Activates AMPk to promote improved blood sugar control and metabolism.
- Health benefits and safety confirmed in human double-blind, placebo-controlled studies.
- Supports weight loss

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Allulose Monk from Doctor Murray

Advantages:

- True 1:1 to sucrose
- Measures like sugar
- Best mouthfeel
- Zero aftertaste
- Zero calories
- Superior granulation
- Super clean!
- Non-GMO
- Best value!!!

PGX® (*PolyGlycopleX*)

Benefits:

- Patented soluble fiber matrix with exceptional viscosity.
- Enhanced physical and physiological effects of soluble fiber.
- Binds more than 600 times its weight in water.
- Produces clinical results at practical dosages.
- Exceptional scientific portfolio of safety and effectiveness.

PGX Provides Unique Benefits

Detailed scientific investigations have shown PGX to exert the following benefits:

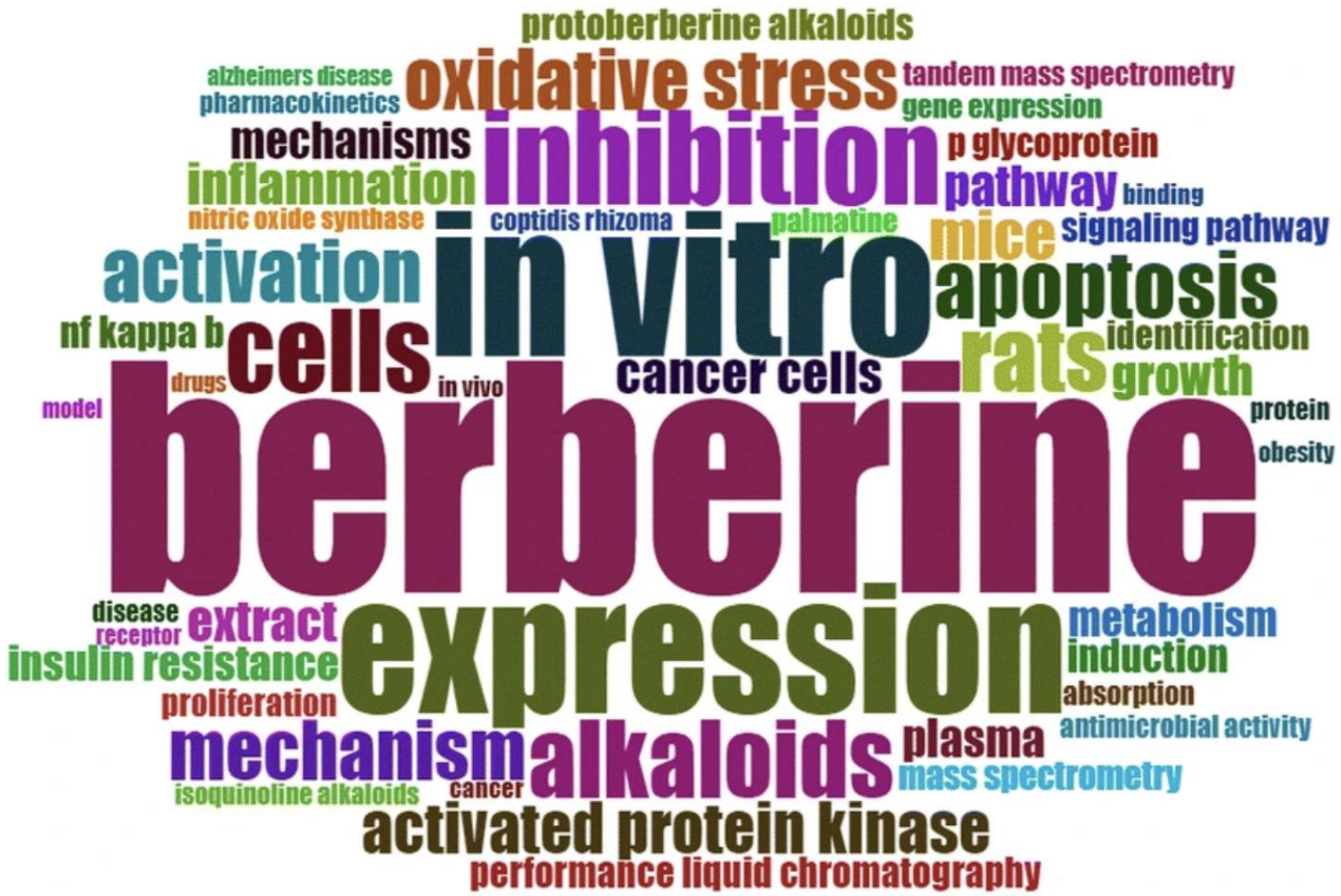
- Reduces appetite and promotes effective weight loss
- Increases the level of compounds that block the appetite and promote satiety including GLP-1
- Decreases the level of compounds that stimulate overeating
- Reduces postprandial (after-meal) blood glucose levels when added to or taken with foods
- Reduces the glycemic index of any food or beverage.
- Increases insulin sensitivity, decreases blood insulin levels
- Improves blood sugar control
- Stabilizes blood sugar levels in the overweight and obese
- Lowers blood cholesterol and triglycerides

Practical Matters with PGX

- Dosage
  - 1 to 2.5 grams before meals for glycemic effect
  - >5 grams before meals for satiety and weight loss
- Side Effects
  - Flatulence and/or looser stools initially in about 10% of patients
- Drug Interactions
  - Take medications one hour before or after PGX
- Nutrient Interactions
  - Does not affect net nutrient absorption

Word Cloud for Berberine Research 1985-2018

From: The status of and trends in the pharmacology of berberine: a bibliometric review [1985–2018]



Word cloud of the top 50 words

Berberine as a Weight Loss Aid

Meta-analysis of 12 Double-blind Trials

Results:

Berberine treatment moderately but significantly decreased body weight (WMD = -2.07 kg, body mass index (BMI) (WMD = -0.47 kg/m2), waist circumference (WC) (WMD = -1.08 cm) and CRP (WMD = -0.42 mg/L).

Conclusion:

This meta-analysis found a significant reduction of body weight, BMI, WC and CRP levels associated with berberine intake which may have played an indirect role in improved clinical symptoms in diseases with metabolic disorders.

Clin Nutr ESPEN. 2020 Aug:38:43-49

berbevis™

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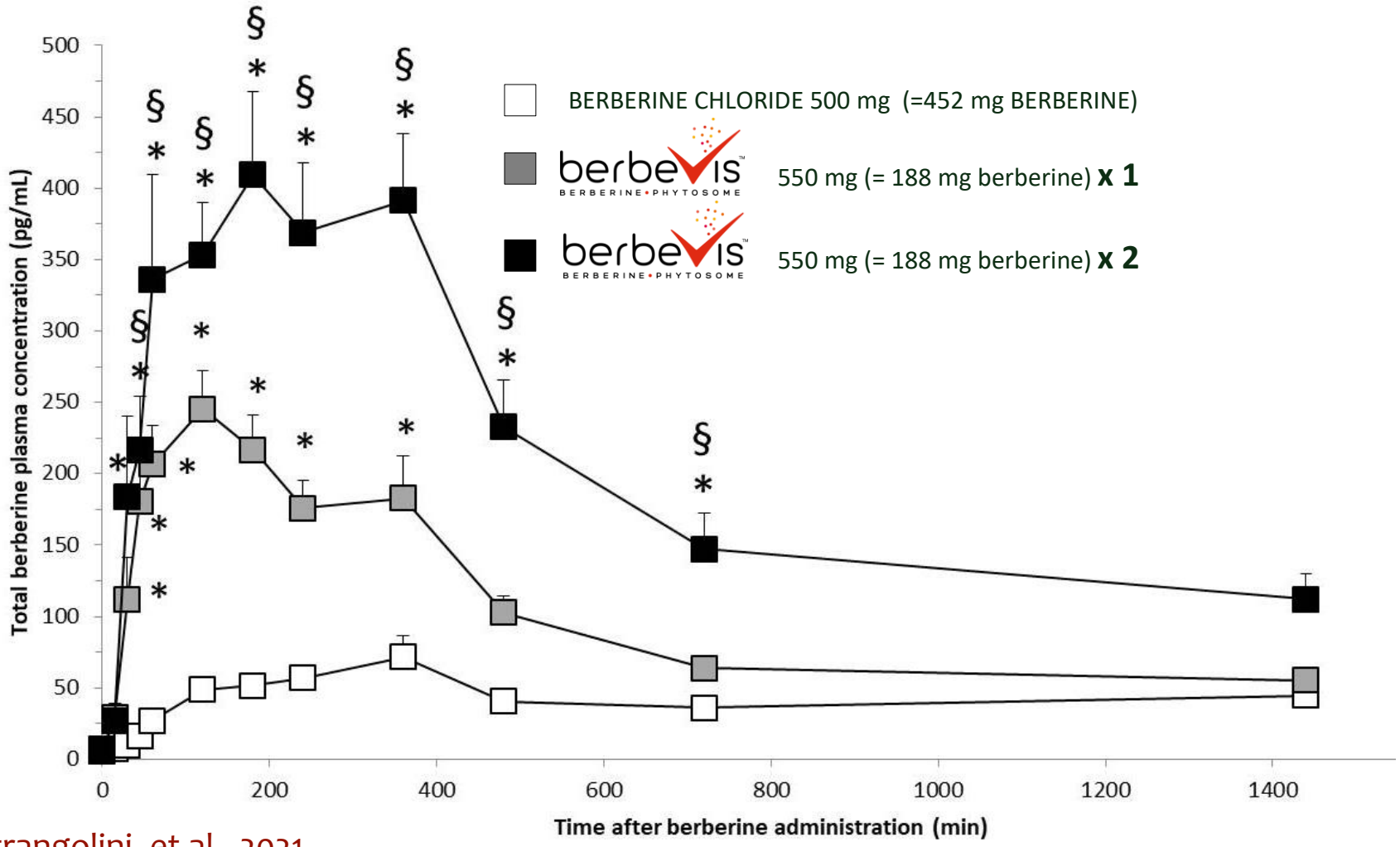
Berberine Phytosome for Improved Results



Giovanna Petrangolini, et al., 2021.

berbevis™

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Berberine Phytosome in Overweight Prediabetics

Summary:

After two months of treatment a statistically significant difference between Berbevis (550 mg twice daily) and placebo groups was observed for glycemia [-12], total cholesterol (-8%], total cholesterol/HDL [-12], triglycerides [-9%],], ApoB/ApoA [-15%], insulin [-29%], visceral adipose tissue (VAT) [-11%] and fat mass [-6%].

Eur Rev Med Pharmacol Sci. 2023 Jul;27(14):6718-6727

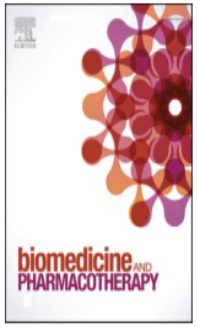
Berberine Improves Metabolism Based on Gut Microbiome Actions

Biomedicine & Pharmacotherapy 139 (2021) 111595

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha



Original article

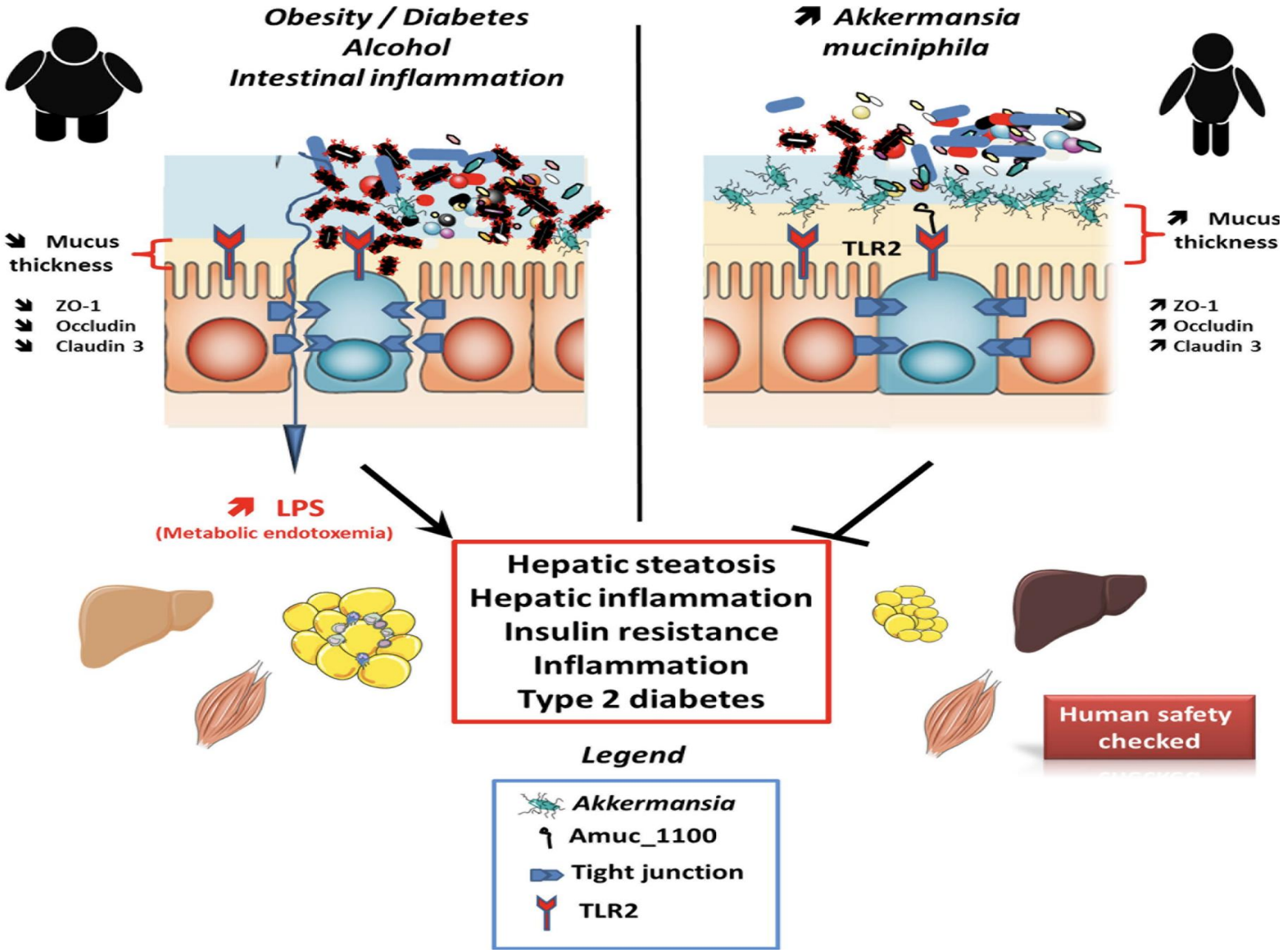
Berberine, a potential prebiotic to indirectly promote *Akkermansia* growth through stimulating gut mucin secretion

Chaoran Dong [b,1], Jiaqi Yu [a,1], Yanan Yang [a,1], Fang Zhang [a], Wenquan Su [c], Qinhua Fan [c], Chongming Wu [a,*], Shengxian Wu [c,*]

Akkermansia muciniphila:

A True Intestinal Superstar

- Critical to the health of the mucin layer that protects the intestinal lining and maintains proper structure of the intestinal lining.
- Levels inversely affect rates of obesity, diabetes, inflammation, and metabolic disorders.
- More effective as heat-killed vs. live.
- A protein, Amuc_1100 is a "postbiotic" – defined as either a metabolite or a liberated cellular structure



Results from a Double-blind, Human Study with Akkermansia muciniphila

Study: Depommier C, et al. Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study. Nat Med. 2019 Jul;25(7):1096-1103.

Summary: 32 subjects with metabolic syndrome were given placebo, or live or heat-killed *A. muciniphila* for 3 months. Compared with placebo, insulin sensitivity increased while total cholesterol and some markers of inflammation and liver function improved. There was also a significant decrease in the white blood cell (WBC) count in those who got the bacteria. **The heat-killed bacteria outperformed the live bacteria** because removing the protective exoskeleton liberates the protein Amuc_1100.

Enhancing the Growth of A. muciniphila

- **Digestive enzymes**, especially if insufficient endogenous secretion or activity.
- Prebiotic fermentable dietary fiber such as **PGX**, inulin, various oligosaccharides (fructo-, malto-, and xylo-), pectin, tapioca fiber, acacia gum and resistant dextrin.
- **Fish Oils**
- **Berberine** is helpful especially in those with metabolic syndrome, diabetes, or obesity.
- **Oleoylethanolamide (OEA)**
- Flavonoid and polyphenol rich foods, beverages, and extracts such as **Morosil®**

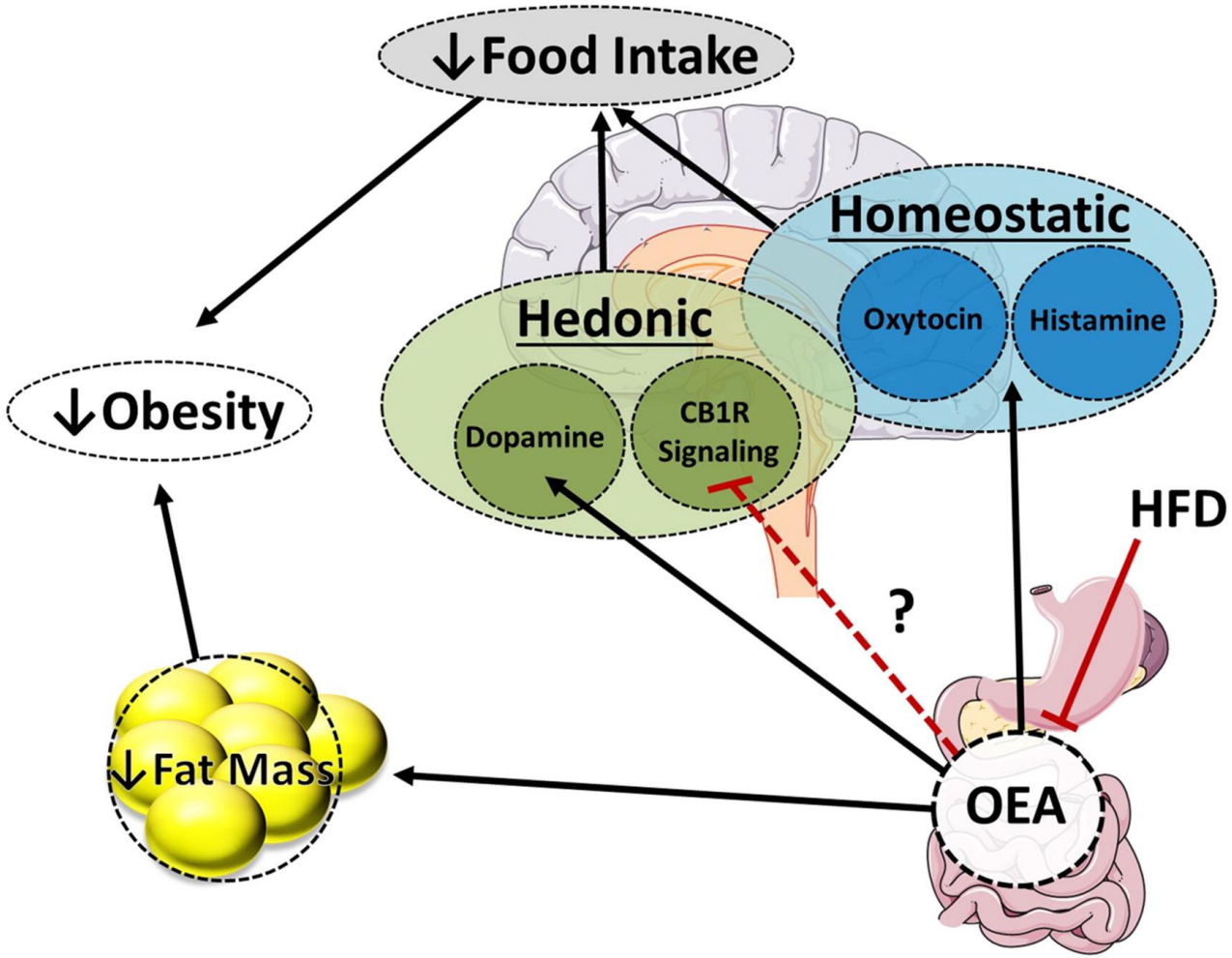
What is Oleoylethanolamide (OEA)?

OEA is a compound the body manufactures that has a high affinity to bind to a receptor in the nucleus of the cell (PPAR-α) that regulates many cellular processes including inflammation. OEA exerts important physiological and metabolic action through the endocannabinoid system.

In a nutshell, OEA exerts anti-depressant activity, controls appetite and satiety, stimulates the breakdown of fat cells, and promotes the burning of fat as energy. The satiety-inducing effects occur by activating specific areas in the brain and the release of the love hormone oxytocin.

Clin Exp Pharmacol Physiol. 2019 Dec 23.
https://onlinelibrary.wiley.com/doi/abs/10.1111/1440-1681.13238

OEA MECHANISMS OF ACTION



Peptides 49 (2013) 21–26

Contents lists available at ScienceDirect

Peptides

journal homepage: www.elsevier.com/locate/peptides

Short communication

The satiety signal oleoylethanolamide stimulates oxytocin neurosecretion from rat hypothalamic neurons

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ABSTRACT

The anandamide monounsaturated analogue oleoylethanolamide (OEA) acts as satiety signal released from enterocytes upon the ingestion of dietary fats to prolong the interval to the next meal. This effect, which requires intact vagal fibers and intestinal PPAR-alpha receptors, is coupled to the increase of c-fos and oxytocin mRNA expression in neurons of the paraventricular nucleus (PVN) and is prevented by the intracerebroventricular administration of a selective oxytocin antagonist, thus suggesting a necessary role of oxytocinergic neurotransmission in the pro-satiety effect of OEA. By brain microdialysis and immunohistochemistry, in this study we demonstrate that OEA treatment can stimulate oxytocin neurosecretion from the PVN and enhance oxytocin expression at both axonal and somatodendritic levels of hypothalamic neurons. Such effects, which are maximum 2 h after OEA administration, support the hypothesis that the satiety-inducing action of OEA is mediated by the activation of oxytocin hypothalamic neurons.

Oleoylethanolamide (OEA) in Obesity:
Double-Blind Clinical Trial

Study Design:

60 obese subjects were given 125 mg OEA or placebo twice daily for 60 days.

Results:

Weight, body mass index, waist circumference, and fat percent decreased significantly at the end of the study in the OEA group ($p < 0.01$). Hunger, the desire to eat, and cravings for sweet foods also decreased significantly ($p < 0.01$). Quantitative real-time PCR analysis showed significant increase in PPAR-α gene expression with OEA.

Appetite. 2018 Sep 1;128:44-49.

Oleoylethanolamide (OEA) in Obesity:

Appetite. 2018 Sep 1;128:44-49

Variables	OEA group (n = 27)	Placebo Group (n = 29)
Weight (kg)		
Before	93.0(13.2)	91.2 (13.6)
After	91.8 (13.1)	91.7 (13.5)
BMI (kg/m^2)		
Before	34.7 (2.4)	35.1 (2.8)
After	34.4 (2.5)	35.4 (2.8)
Waist circumference (cm)		
Before	105.3 (13.8)	102.5 (10.5)
After	100.6 (14.5)	103.0 (11.6)

MOROSIL™

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MOROSIL™ is a standardized powder extract obtained only from the juice of the Moro unique cultivar of blood oranges from Sicily

Moro Red Orange *is the most colorful of the blood oranges. The flavor is stronger and the aroma is intense. The 'Moro' variety is believed to have originated at the beginning of the 19th century in Sicily.*

The **PHYTOCOMPLEX** contained in Moro juice, unlike other orange varieties, have been shown to possess a high content of anthocyanins with an important activity against fat accumulation and obesity.

COMPOSITION	MOROSIL™ % (W/W)
Anthocyanins (cyanidin-3-glucoside)	0.8 – 0.9
Hydroxycinnamic acids (caffeic, cumaric, sinapic, ferulic, cinnamic)	0.8 – 1.0
Flavanones (hesperidin, narirutin)	2.0 – 2.2
Ascorbic acid	4.3 – 4.5

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Double-blind, clinical trial

DESIGN:

Randomized, Double-blind, Placebo controlled trial conducted in Australia;

- N= 102 overweight (25<BMI<30) healthy adults (male and female, aged 20-65) including Asians;
- 400mg of **MOROSIL™** or placebo for 6 months;

AIM:

To assess the effect of **MOROSIL™** on weight loss in overweight adults in conjunction with calorie restriction diet and exercise* over a 6-month period.

ENDPOINTS:

- Weight loss;
- BMI;
- Hip and waist circumference;
- Changes in body composition (DEXA).

Nutrients 2022, 14, 427

MOROSIL™

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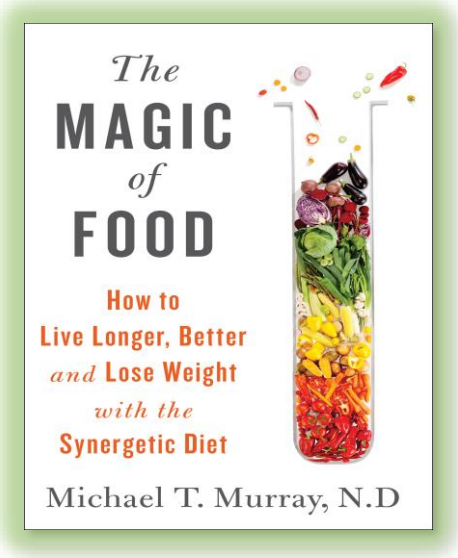
Results in a double-blind, clinical trial

The MOROSIL™ supplementation lead to a change in the fat body composition: there was a statistically significant decrease in the abdominal, visceral and subcutaneous fat mass, while the lean mass was kept constant.

		3 MONTHS	6 MONTHS
BODY WEIGHT	MOROSIL™	↓ -3,3%	↓ -4,2%
	Placebo	↓ -2,1%	↓ -2,3
WAIST CIRCUMFERENCE	MOROSIL™	↓ -2,5%	↓ -3,6%
	Placebo	↓ -2,3%	↓ -2%
HIP CIRCUMFERENCE	MOROSIL™	↓ -2,1%	↓ -2,8%
	Placebo	↓ -1,7%	↓ -1,9%

Nutrients 2022, 14, 427



Instagram @dr.michaelmurray

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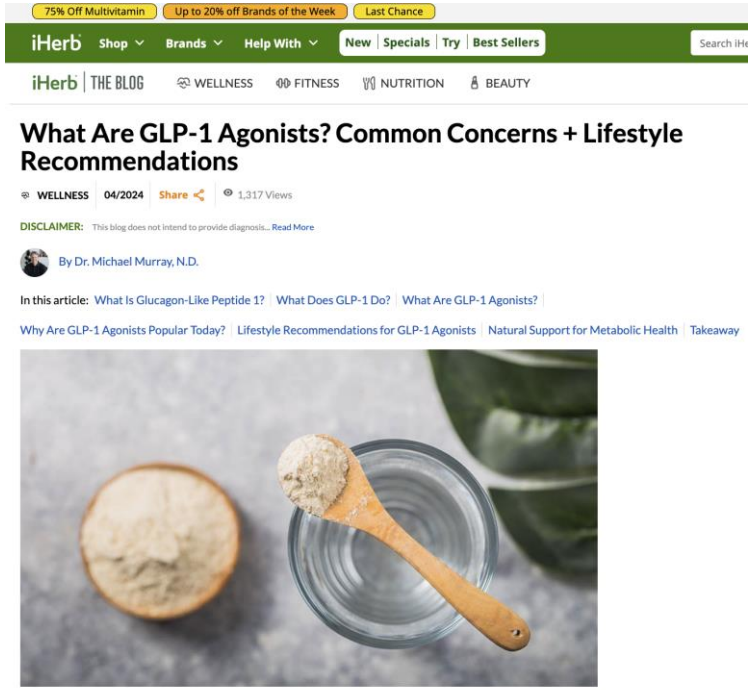
For more information

Thank You!!!



https://www.iherb.com/blog/glp-1-agonists-support/1890