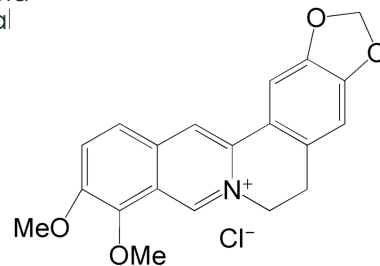




What is Berberine?

Far more than the latest trend!

- Berberine is a bright yellow isoquinoline alkaloid derived from the roots and rhizomes of several plants.
- Several plants are rich sources of berberine alkaloids including:
 - Barberry (*Berberis vulgaris*, *Berberis aristata*)
 - Oregon Grape (*Berberis aquifolium*)
 - Goldenseal (*Hydrastis canadensis*)
 - Chinese Goldthread (*Coptis chinensis*)
- Berberine was first isolated in 1917 from Goldenseal.



What is Berberine?

- When we see **Berberine HCL** that indicates it is the alkaloid only, not the whole plant.
- While berberine alkaloids can be sourced from many plants, the majority of berberine on the market today is derived from Barberry.
 - Abundant, sustainable supply
 - High yield
- There are as many as 500 species of Barberry
 - Also known as Indian Barberry, the aristata and vulgaris are commonly used for medicinal purposes.
 - Grows abundantly in the Himalayas
 - Not on any endangered watch lists



CITES The Convention on International Trade in Endangered Species of Wild Fauna and Flora is an international agreement between governments.



International Union for Conservation of Nature (IUCN) Red List: comprehensive information on the global conservation status of all known species.

3

History and Use

- Berberine has over 3,000 years of history in TCM, Ayurveda, and European traditional medicine.
 - Long history of safety
- The majority of historic use references:
 - Antimicrobial support*
 - Healthy gut tissue*
 - Diarrhea*
 - Cardiovascular support*
- In more recent years, berberine has become well known for its impact on healthy blood sugar regulation and metabolic function.*



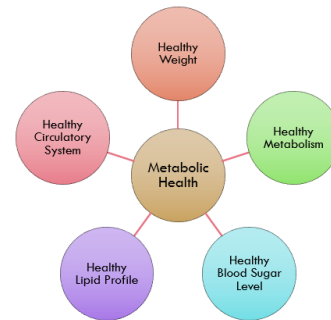
<http://herbalgram.org/resources/herbclip/herbclip-news/2020/barberry/>

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4

Modern Clinical Trials

- In 2015, a meta-analysis was performed on 27 randomized controlled clinical trials which included 2569 patients.
- Sources for studies included:
 - Center for Primary Care & Integrative Medicine, Houston TX
 - Cincinnati Children's Hospital Medical Center, Cincinnati OH
 - Wenzhou Hospital of Traditional Chinese Medicine, Wenzhou China
- Results indicated that berberine had meaningful impact on several facets of metabolic health.*



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8107691/>

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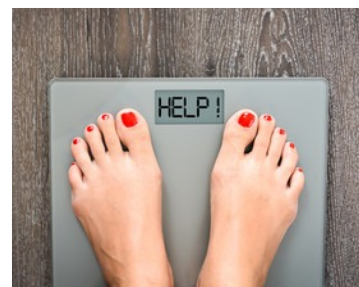
5

The Obesity Epidemic

New research finds that **by 2030, nearly half of American adults will be obese.**

Today:

- **Nearly 1 in 3 adults are overweight**
- **42% have obesity**
- **9% have severe obesity**



Obesity is defined as having a BMI over 30



And it's not for lack of effort...

<https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity>

6

Healthy Blood Sugar

1 in 3 Americans experience problems with **healthy blood sugar metabolism**. Same percentage as the amount that are overweight!

Sugar addiction is real!

These cravings are a **major impediment** when trying to stick to a **healthy diet**.

Berberine is a **time-tested herbal ally** to help get back on track with a **healthy eating plan** and is **clinically studied** to support **healthy blood sugar** already within normal range.

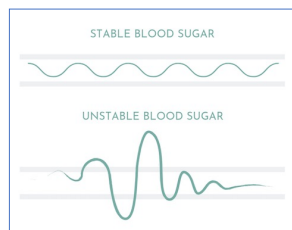
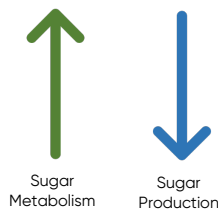


<https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2410027/>

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Healthy Blood Sugar*



- Supports healthy insulin sensitivity*
 - Study of individuals with metabolic syndrome took 3/ 500 mg. Berberine HCL capsules per day in divided doses for 90 days.
 - Compared with placebo group, Improvements in healthy waist circumference, blood pressure and insulin sensitivity were shown.*
- Boosts healthy glycolysis (sugar metabolism), which helps your body utilize sugar properly*
- Modulates normal gluconeogenesis (sugar production in the liver).*

<https://pubmed.ncbi.nlm.nih.gov/23808999/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491964/>

<https://www.researchgate.net/publication/322700144>

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Metabolic Master Switch



- **Berberine activates** a **metabolic enzyme** called **AMPK** (Adenosine Monophosphate-Activated Protein Kinase).
- This **enzyme** is sometimes referred to as the “**metabolic master switch**.”
- It is found in every cell of the body and plays a **major role** in **supporting healthy metabolism**.*
- Other ways to **trigger AMPK** that are very popular:
 - Fasting (intermittent and sustained)
 - Vigorous Exercise
 - Cold plunge/hot sauna
- These are examples of temporary stressors on the body which spur it into a healing state.



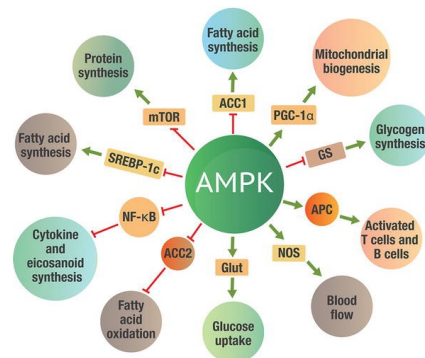
More on AMPK...

<https://diabetes.diabetesjournals.org/content/55/8/2256.full>

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AMPK Activation

- **AMPK is activated in response to stressors** (low glucose, heavy exertion, temperatures) that deplete cellular ATP supplies.
- As a cellular energy sensor responding to low ATP levels, **AMPK activation positively regulates signaling pathways that replenish cellular ATP** which is required for autophagy.
- Activated **AMPK stimulates energy generating processes** such as glucose uptake.



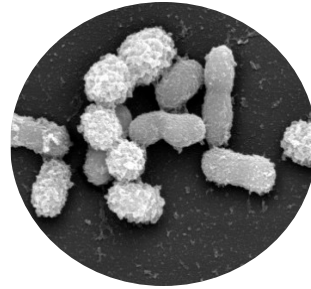
<https://www.cellsignal.com/pathways/ampk-signaling-pathway>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2779044/>
<https://www.intechopen.com/chapters/81304>

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Gut Bugs and Waistlines

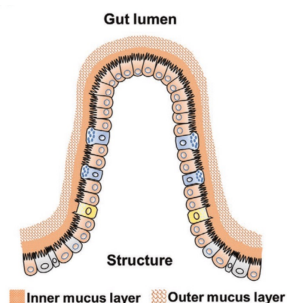
- *Akkermansia muciniphila* is a native gut bacteria that should make up **3-5% of the human microflora**.
 - Numerous studies have shown a positive correlation between robust *Akkermansia* populations and decreases in metabolic syndrome, obesity, and age associated mental decline.
- *Akkermansia* supports mucin secretion AND feeds on our gut's intestinal mucosal layer. As a byproduct of munching on mucin, **short-chain fatty acids (SCFAs)** including **butyrate** are created.
 - Butyrate is vital energy source for mucus-secreting cells and intestinal epithelial cells.
- **SCFAs also strengthen tight junctions in the intestines.**
 - This is why *Akkermansia* is effective as a preventative for many conditions. As a result of strengthened junctions, unwanted materials are not passing through the intestines and the normal inflammation responses which can eventually run amok are curtailed.
 - Downregulates pro-inflammatory cytokines TNF- α , IFN- γ



<https://www.ncbi.nlm.nih.gov/pubmed/29202334>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6064808/pdf/jcbn18-57.pdf>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6485276/>

11

Akkermansia Muciniphila



- In the dysregulated sugar imbalanced state, the breakdown of the intestinal mucosal barrier modifies the pathological condition; it has been shown that *Akkermansia* promotes mucus secretion and makes the barrier mechanism more robust.
- It has also been demonstrated that *Akkermansia* is involved in the immune response, specifically the production of IL-10; a regulatory cytokine.

<https://pubmed.ncbi.nlm.nih.gov/29472701/>
<https://pubmed.ncbi.nlm.nih.gov/27892954/>

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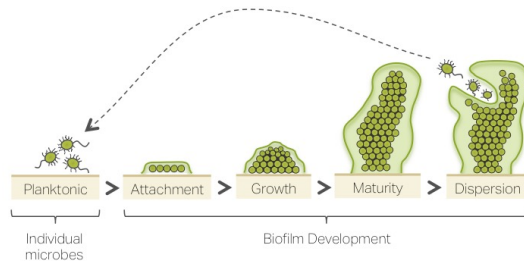
Dysbiosis

Definition of Dysbiosis:

Dysbiosis is defined by an imbalance in bacterial composition, changes in bacterial metabolic activities, or changes in bacterial distribution within the gut. The three types of dysbiosis are:

1. Loss of beneficial bacteria
2. Overgrowth of potentially pathogenic bacteria
3. Loss of overall bacterial diversity

Biofilm Lifecycle:



Berberine has been long used for healthy gut for good reason!
The combination of the alkaloids and the promotion of good bacteria via mucin promote healthy, long term microbiome integrity.*

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4840435/>

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Berberine Recap:

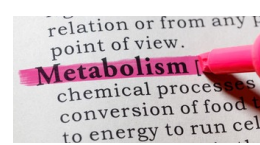
Three Key Actions:

1. **Supports healthy blood sugar** levels while making it **easier to kick the sugar habit***
2. **Activates AMPK** – the metabolic ‘**master switch**’ enzyme*
3. **Enhances the gut bacteria Akkermansia** which is known to **support glucose metabolism** and **healthy body fat percentage***



Sounds just about perfect, except...

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Berberine Is A Fantastic Remedy With A Few Challenges:

Low bioavailability. While still being effective, less than .5% of the berberine alkaloids are typically found in the blood.

To offset this, **large doses** are often **needed to achieve results**.

Large doses can cause **uncomfortable detox** or **irritate intestinal lining** and may **not be tolerated well**.



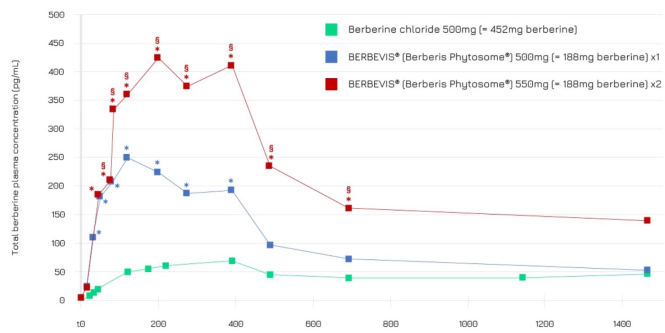
What if we could solve these challenges?

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Berberine Bioavailability – Solved!

**Berberine
Phytosome
Delivers
9.6X
Better
Bioavailability!**

Human pharmacokinetic study results:



How does the Phytosome work?

What Is The Phytosome Made Of?

Phytosome technology chaperones the active botanical substance across cell membranes and into the cell, producing far superior bioavailability.

Berberis® is the trademark name for the Berberine Phytosome.

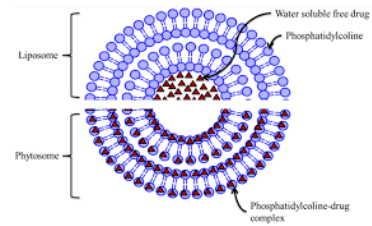
Pea Protein and Grapeseed Extract

• Why Pea Protein?

- **Whole Berberine root extract** in the presence of **protein** showed **better intestinal absorption** and enhanced presence in plasma.
- Pea protein is **well tolerated and low allergen**.

• Why Grapeseed Phytosome?

- Grapeseed within the phytosome matrix provides antioxidant activity which **supports gastrointestinal cells** and **enhances tolerability**.*
- The **fat in the phytosome** is a small amount of **sunflower oil** – preferable to the often used, soy oil.



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Healthy Reduction In Body Fat*

PARAMETER	BASELINE	30 DAYS		60 DAYS	
	VALUE	VALUE	% VARIATION vs BASELINE	VALUE	% VARIATION vs BASELINE
BMI	25.39	24.7	-3%	24.57	-3%
VAT (g)	456.92	383.5	-16%	357	-22%
WAIST CIRCUMFERENCE (In)	39.66	39.00	-2%	38.38	-3%
HIP CIRCUMFERENCE (In)	41.73	41.13	-2%	40.98	-2%
Waist/Hip Ratio (%)	0.83	0.83	0%	0.83	-1%
Total Mass (Lbs)	150.65	147.10	-2%	145.46	-3%
Fat Mass (Lbs)	57.64	55.65	-4%	53.86	-7%

berbevis
BERBERINE PHYTOSOME

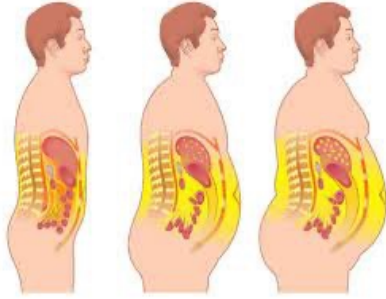
Note: Study results based on therapeutic dose of 4 caps per day (2 caps 2x/day)

**HAD A POSITIVE EFFECT ON BODY COMPOSITION, INDUCING A REDISTRIBUTION OF ADIPOSE TISSUE
EVEN IF ENROLLED SUBJECTS WERE NOT UNDER LOW CALORIES DIET**

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What is VAT?



Healthy visceral fat is white adipose tissue that is stored in the **abdominal cavity**.

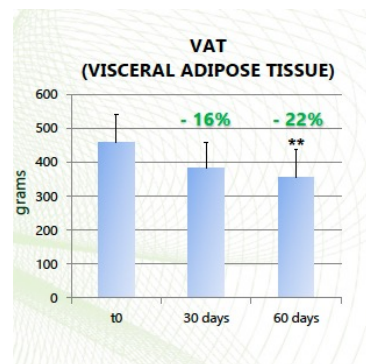
However, **increased visceral fat deposits** associated with **obesity** are linked to **metabolic disorders** and **excessive cytokine production**.

Visceral fat contains an **enzyme** called **aromatase**, which **converts testosterone into estrogen**.

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VAT: “Active Body Fat”

- Visceral adipose tissue is a **hormonally active component of total body fat**, which possesses unique biochemical characteristics.
- **VAT secretes hormones** that can lead to higher inflammation levels, creating an environment for conditions associated with metabolic syndrome such as:
 - Obesity
 - Heart disease
 - High cholesterol
 - Type 2 diabetes



22% reduction in 60 days without dietary intervention!

Note: Study results based on therapeutic dose of 4 caps per day (2 caps 2x/day)

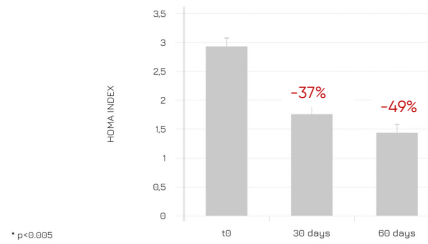
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Healthy Blood Sugar*

- After 30 days of treatment there was a meaningful impact on healthy insulin activity.*
 - The homeostatic model assessment (HOMA) is a mathematical formula correlating blood glucose and insulin. It's a validated method used to quantify insulin resistance and function of pancreatic beta-cells (which produce insulin).
- The higher is the HOMA score, the higher is the risk of insulin resistance.

Parameter	Baseline	30 days	60 days
HOMA	2.88	1.81	1.47



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Berberine Recap:

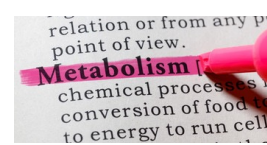
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There IS a Place For Both!

Recommended Use: 1 capsule with meals, three times a day. Consult with physician prior to use if you are pregnant or nursing, taking medications or have a medical condition.

Caution: This product is not intended for individuals with impaired glucose metabolism such as prediabetes or diabetes.

Supplement Facts
Serving Size: 1 Capsule
Servings Per Container:

Amount Per Serving	%DV
Berberine HCl (95%) (from <i>Berberis aristata</i>) (bark & roots)	510 mg **
Leucine	50 mg **

** Daily Value (DV) not established



- Three caps per day
- Potency in line with current consumer understanding

Recommended use: 1 capsule before meals with a glass of water, twice a day. Consult with physician prior to use if you are pregnant or nursing, taking medications or have a medical condition.

Caution: This product is not intended for individuals with impaired glucose metabolism such as prediabetes or diabetes.

Supplement Facts
Serving Size: 1 Capsule Servings Per Container: 60

Amount Per Serving	%DV
Berberis® Berberine Phytosome.....	275 mg **
from the roots of <i>Berberis aristata</i> standardized to contain 28%~34% of berberine	

** Daily Value (DV) not established



- Two caps per day – smaller capsule
- Lower potency but higher bioavailability



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Berberine – The Master Metabolism Herb!



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