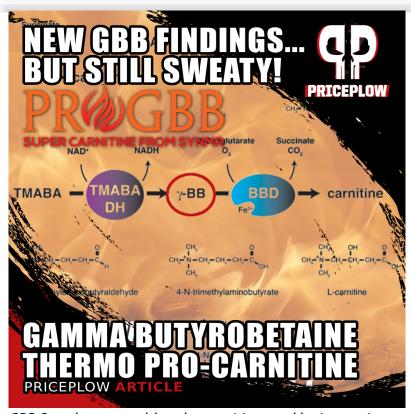
GBB (Gamma-Butyrobetaine Ethyl Ester): Super Carnitine That Makes You Sweat?!

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If you follow PricePlow, you've likely tried a **carnitine**-based supplement in the past. We love L-carnitine supplements — there's an incredible amount of data supporting them for metabolism, performance, recovery, and overall health. But sometimes we're looking for a *different* way to approach a situation, want different effects, or are simply looking for a smaller dosage.



GBB Supplements add to the carnitine pool by increasing the reagent — GBB — which goes on to make more carnitine if your body needs it! But the experiential part is its thermogenic effect that makes many users sweat more during workouts!

That's what we get from *GBB*, short for **gamma**– **butyrobetaine**, the new kid on the carnitine block that made major waves in the dietary supplement industry in the 2010s and still continues to thrive in the weight loss space to this day.

The short goes like this:
GBB is a *carnitine precursor*,
helping to support the
body's own carnitine

precursor, helping to support the body's own carnitine production, supporting many of carnitine's functional benefits. But beyond that, it's well known to leave you sweating more than anything you've ever felt.

Dive into this post to find out if this pro-carnitine ingredient is right for you, and what's happening when you take it!

This article has been updated in 2024 to include new research that's been published surrounding the ingredient. Our conclusions remain the same: it's a novel way to boost carnitine content at lower doses, but with its well-known thermogenic effect!

GBB Supplement Summary

GBB, or *Gamma-Butyrobetaine ethyl ester HCl*, is the molecule that your body converts into L-Carnitine when naturally producing its own carnitine.

• Pro-Carnitine: Studies show that GBB supplementation can increase the body's plasma L-Carnitine levels by nearly double! Thus, its benefits are similar to the benefits of carnitine



supplementation, which depend on the user's diet and carnitine status.

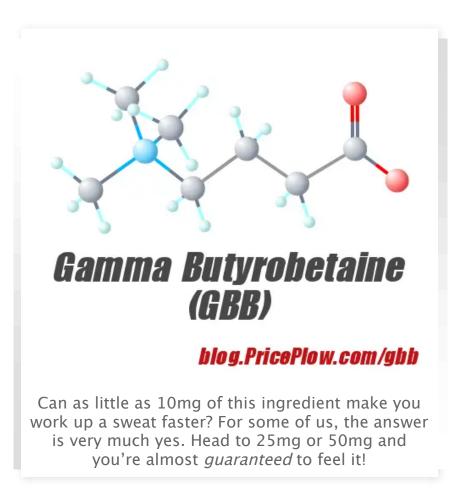
- Thermogenic! For a still-undetermined reason (we have theories), GBB causes a serious amount of thermogenesis and *sweating*, especially if taken pre-workout, so it's included in many popular thermogenic carnitine liquids, fat burners, and weight loss aids.
- **Dosage:** The typical dose is *10–20mg twice daily*, and right now our conservative daily max is 50mg, although

many have gone higher and studies have tested *far* higher. The higher you go, the more extreme the effects get – 50 milligrams generally provides some serious sweating.

- **Featured GBB Supplements**: There are several ways to use GBB, so it first depends on your form factor:
 - Fat Burning Powder.
 For a heated, energy-based fat burning drink, we've been incredibly impressed with SteelFit Steel
 Sweat.
 - Stimulant-Free Fat Burning Powder: AstroFlav Drip has a perfect 20mg GBB to get the sweat going.
- Trusted Ingredient: We've tested and trusted *ProGBB*, which is manufactured by *SYNMR Biotechnologies*. Read more at <u>SYNMR.com</u> (and see the <u>ProGBB lab tests</u> lower on this page)
- Combating Deficiency: New research has shown that individuals with mood disorders are significantly lower in serum GBB. This has been known with L-carnitine, but now we can add GBB to the situation as well.
- **Safety:** Safety studies even include *infants*, and GBB is theorized to be *safer* than carnitine supplements at these doses because there's no chance of it turning into the toxic D-Carnitine isomer, which could potentially be in some poorly-sourced carnitine supplements.

Up-Front: What are the typical GBB "claims"?

The *purpose* of this post is to educate and investigate the science on **GBB**, a relatively new soldier on the supplement ingredient chess board. GBB is an ingredient we've seen in numerous fat burners since about 2015. While there are several claims made about the benefits of GBB, brands usually use it as a "sweat amplification" agent, sometimes marketing it *for* the sweat generated during training sessions.



A few clinical trials show
GBB to be a formidable
ingredient for the industry
and certain types of dieters.
The most impressive
amongst these claims is a
study showing a *near- doubling* of plasma
carnitine levels after
supplementation, and an
increase of 300% carnitine
excretion.^[1,2]

It's often advertised that GBB will function similarly to other carnitine

supplements... but the ingredient takes it a step further due to its ability to raise plasma levels so incredibly high.

Further, GBB supports the body's own *endogenous* carnitine production, so it can be paired with supplemental *(exogenous)* L-carnitine to cover both angles. This method of combining precursors *with* the targeted substrate is popular in the supplement industry, since it provides a backstop for those who may have metabolic or absorption issues due to poor gut or liver health.

The recommended dosage of GBB is what sets it apart from other forms of carnitine supplements. While industry veterans like acetyl-l-carnitine (ALCAR) or l-carnitine-l-tartrate (LCLT) typically require doses closer to a gram (and preferably *two* grams), GBB works similarly to other forms of carnitine in far lower doses like **50mg per day**. This is a huge win for GBB, as high doses of other carnitine supplements take up too much space (disadvantageous in a capsule) and simply cost more.

	Diet supplement, d 11-20			
Day	Lysine + Methionine $n = 6$	ϵ -N-Trimethyllysine $n=5$	γ -Butyrobetain $n = 5$	
	n - 6	<u> </u>	<i>H</i> - 3	
		n m ol/ml		
2	44.1 (6.8)	3 9.3 (10.4)	50.2 (6.9)	
4	45.5 (8.3)*	42.6 (7.8)	45.4 (3.0)	
6	43.3 (8.9)	39.2 (9.1)	48.6 (11.6)	
8	40.2 (8.3)	38.6 (3.4)	50.2 (10.1)	
10	40.3 (7.7)	42.0 (7.3)	50.1 (10.5)	
12	38.1 (9.2)	46.0 (6.6)	80.8 (15.8)*	
14	41.4 (8.2)	47.3 (6.5)	89.4 (16.6)	
16	42.7 (7.7)	53.4 (7.3)*	87.0 (20.2)*	
18	44.9 (7.7)*	52.3 (6.5)*	87.9 (13.7)*	
20	41.8 (7.5)	56.0 (7.8)*	88.7 (14.3)*	

An early study on carnitine's precursors showed that GBB (to the right) is the best of the bunch at increasing plasma carnitine levels. [1]

"Super Carnitine"?

Because of the above data, many companies market GBB as a "super carnitine". It has *clinical* research backing its safety, a low active dose, and raises carnitine levels in the body higher than other supplements.

However, there wasn't much *serious* research published online about the ingredient, so we dug up every scientific paper possible on GBB to see if these "super carnitine" claims were true. Here's what we found:

What is GBB?

The story on GBB really starts with the end–goal: more L–carnitine. **Carnitine** is a low molecular weight, water–soluble, bioactive amino acid whose L–isomer (L–carnitine) has long been known to participate in the process of lipid metabolism. ^[3] Its many benefits are covered later in this article, but needless to say, it's *conditionally essential* — while the body can generate some of its own, most needs to come from diet or it will not function properly. ^[4]

Gamma-butyrobetaine

(GBB) is a carnitine *precursor* that eventually gets converted *into* L-carnitine. GBB is converted to L-carnitine through an enzyme named *Gamma-butyrobetaine dioxygenase* (also known as *BBD* or BBOX). [5-7] "GB

dioxygenase", as the name implies, is an oxidoreductase enzyme, [8]

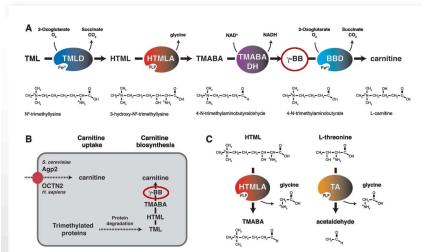


Figure 2. The enzymes of the carnitine biosynthesis pathway and their contribution to cellular carnitine homeostasis. (A) Enzymatic conversions of the carnitine biosynthesis pathway. TML: N6-trimethyllysine, TMLD: TML dioxygenase, HTML: 3-hydroxy TML, HTMLA: HTMLA aldolase, TMABA: 4-N-trimethylaminobutyraldehyde, TMABADH: TMABA dehydrogenase, γ-BB: 4-N-trimethylaminobutyrate, BBD: γ-BB dioxygenase, PLP: pyridoxal 5'-phosphate. (B) schematic representation of carnitine uptake and biosynthesis. Carnitine uptake is mediated by the OCTN2 transporter in humans or the Agp2 transporter in S. cerevisiae. Degradation of proteins containing trimethylated lysine residues results in availability of TML as a substrate for intracellular carnitine biosynthesis. (C) Comparison of the enzymatic reaction catalyzed by HTMLA and threonine aldolase (TA). Both enzymes perform a similar aldolytic cleavage of their substrate into glycine and an aldehyde (TMABA and acetaldehyde for HTMLA and TA, respectively).

The Carnitine Biosynthesis Pathway. [5] GBB, or YBB, is circled in red.

and these enzymes facilitate conversions through electron movement. This is the final step in endogenous carnitine biosynthesis.

Supporting endogenous carnitine production

Researchers generally claim that 75% of L-carnitine comes from the diet, while the other 25% is synthesized endogenously^[9] (this statistic may change based upon diet and we are still working to confirm it). The last step in the endogenous production is conversion from GBB, thanks to support from essential amino acids like lysine and methionine in the brain, kidneys, and liver.^[10]

It's that *endogenous* 25% we're trying to support here. By supplementing with GBB, you provide a "push" for the body to produce more L-carnitine, without forcing customers to eat more red meat, which by far is the best natural source of carnitine.

The rate-limiting precursor?

Research shows that GBBavailability in liver andkidneys is arguably therate-limiting precursor forhuman carnitinebiosynthesis. This issometimes debated, butthe point is that it — andthe BBD/BBOX enzyme —are at least major limitingfactors in endogenous carnitine deficiency. This is much like beta-alanine being the rate-limiting precursor to carnosineproduction for muscular endurance supplements. It thus makessense to supplement some, even if carnitine is more orallybioavailable than carnosine, which necessitates precursors to agreater extent.

The GBB / L-Carnitine Equilibrium

When you add more GBB to the system, you get more carnitine until the levels of both product and reagent balance out. Likewise, if we have more *product*, enzymes can either downregulate to stop the production of more product, or even facilitate the breakdown of product into its constituent parts: more reagents. This allows the body to do its best to never have too much of any one thing. While it is *never* quite this simple in nature, it's the easiest way to think of such reactions.

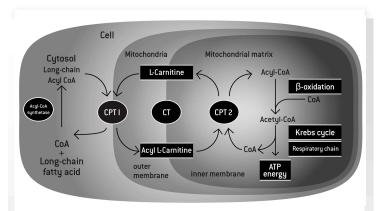


GBB gets converted to carnitine, and vice-versa, until the two compounds reach chemical equilibrium. Excess GBB gets turned into excess carnitine – excess carnitine can potentially get turned back towards GBB.

The pathway images in this article are more detailed than the above simple graphic, but the point is that your body will do its best to maintain *homeostasis* and that this reaction can go in both directions.

GBB supplementation works based on these principles. We add so much material to the left that the reaction goes to the right. It creates more carnitine to balance out the ratio of GBB and I-carnitine in the body. Tyrosine supplementation *also* works by helping conversion reactions move to the product side. This is why it's easier to refer to GBB as a "pro-carnitine" ingredient.

The enzyme for GBB conversion to carnitine is commonly found in the kidney, liver, and the brain, [14-16] with significantly more activity in the kidney. [16] Given the roles of the kidney and liver in fat metabolism, having GBB dioxygenase in these organs makes sense. Carnitine serves an essential role in fat metabolism that will be discussed more below.



"L-carnitine function. I-carnitine shuttles long-chain fatty acids inside the mitochondria by forming a long chain acetylcarnitine ester. The complex is then transported into the mitochondrial matrix by carnitine palmitoyltransferase I (CPT I) and carnitine palmitoyltransferase II (CPT II). The fatty acids are then broken down through the process of β-oxidation to deliver the 2-carbon molecules to the Krebs cycle, leading to the generation of energy under the form of adenosine triphosphate (ATP). In addition, by binding an acetyl group, I-carnitine can maintain the levels of Acetyl-CoA and coenzyme A, playing its buffering role."

Inversely, giving a BBD/BBOX *inhibitor* will *reduce* carnitine levels in cells, and by as

much as 70%!^[6] Here, we're obviously trying to avoid that, but it goes to show how critical this pathway is.

This article assumes you already understand carnitine's benefits. If you don't, you can skip down to the <u>carnitine</u> section, but for everyone else, let's continue to the GBB research:

The leading GBB researcher is Charles J Rebouche, of the Neuromuscular Research Laboratory and Department of Neurology, Mayo Foundation, Rochester, MN. The primary research was conducted in his lab after his team showed that GBB successfully increased L-carnitine concentrations in rodents. But it's the human study where things get wild:

A sweaty situation!

The reason many readers are here is because **GBB** makes most athletes sweat far more than normal. This is often the *main* selling point, as some of us love to sweat when training.

The most commonly-cited research study about the usage of GBB was published in 1989, where 16 participants were given various carnitine precursors for 10 days, after being given a lower-carnitine (no red meat) diet for 10 days beforehand. [1]

GBB Synonyms

The following are known names for GBB:

- 4-Ntrimethylammonium butyrate
- 4trimethylaminobutyrate
- butyrobetaine
- deoxy-carnitine
- deoxycarnitine
- gamma-butyrobetaine

Also note that the gamma character (γ) may be used, such as with γBB or γ -butyrobetaine.

The carnitine precursors given were one of the following:

- L-methionine + L-lysine (6 participants, 75mg/kg each)
- ϵ -N-trimethyllysine (TML) (5 participants, 75mg/kg)
- GBB (75mg/kg, reduced down to 36.5mg/kg)

Right off the bat, we know that the GBB group got a *ridiculously* high dose! We generally max out at 50 milligrams — a standard 175lb man would have received a **6 gram dose**, which was then reduced to *3* grams.^[1] That starting dose is over *100x* what we normally see in the dietary supplement world!

Why did they reduce the dosage? You can only guess:

Participant 12 received 75mg γ -butyrobetaine/(kg body wt-d). The solid inner salt was dissolved in fruit juice or carbonated beverage and consumed in two equal amounts daily at breakfast and dinner.

Because participant 12 complained of excessive sweating and salivation 1–3 h after ingestion of the γ -butyrobetaine supplement, the dosage was reduced to 37.5 mg/(kg body wt-d) for participants 13–16. Only one of these subjects reported any unusual effects (mild increase in sweating on d 11–13) with that dosage of the supplement.^[1]

Those are some wild doses, but they did lead to incredibly increased serum carnitine concentrations: a 60-78% lift!^[1] This was by far more than any other carnitine precursor.

This study also showed that the *BBD/BBOX* enzyme is likely *not* the rate-limiter — the enzyme works plenty fine, so long as there's enough GBB to satisfy it.

With regards to the sweating, however, the scientists don't dig any deeper and fail to suggest a reason why that may have happened. We've seen no explanation *why* this sweating effect occurs, but it's certainly incredibly effective at doing so. You can also rest assured that no dietary supplement is going *anywhere* near what those subjects were taking in the above study.

	Diet supplement, d 11-20				
	Lysine + Methionine	ε-N-Trimethyllysine	γ-Butyrobetain		
Day	n = 6	n = 5	n = 5		
	nmol/mg creatinine				
1-2	181 (60)*	147 (55)	141 (24)2		
3-4	144 (52)	113 (30)	130 (58)		
5-6	146 (43)	100 (18)	99 (36)		
7-8	117 (29)	106 (16)	104 (44)		
9-10	108 (30)	122 (40)	114 (35)		
1-12	131 (53)	173 (47)	3530 (682)*		
3-14	207 (76)*	300 (58)*2	4084 (1225)		
5-16	233 (75)*	389 (58)*	4305 (917)		
7-18	234 (83)*	446 (106)*	4621 (251)*2		
9-20	255 (93)*	477 (67)*	4467 (855)*		
Values are mean $2n = 4$.	(SD) for total carnitine excretion. $^{*}P < 0.05$, co	ompared to value on d 9-10 in the same colu	mn.		

One postulation of ours is that the chemical reaction to get from GBB to Carnitine is exothermic (releases heat), and by triggering the reaction en masse via supplementation, it theoretically outputs the heat. Alternatively, we've wondered if this is a chemically-induced version of the "meat sweats", for those of you who've had such an experience (which is normally blamed on the higher thermic effect of protein).

If we stumble upon an explanation that's *based in actual science*, we'll update this article.

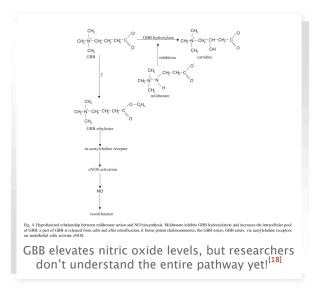
So if that's not enough for the more conservative-minded folks who need to know every mechanism about every ingredient they take, then they may need to wait until more research is done.

GBB leads to nitric oxide enhancement

Another unique aspect of GBB is its consistent impact on nitric oxide levels. [18] At least a few studies have shown GBB to be a

potent vasodilator, but it may require higher doses than most individuals are willing to take.

The sports supplement industry is loaded full of nitric oxide supplements that improve blood flow and workout capacity, and this is another ingredient worth exploring for the right situation. By improving blood flow through increased vasodilation, GBB may help get nutrients to damaged



muscle and joint tissues at a more rapid rate. It may even help keep blood pressure down. GBB has been more consistent in terms of vasodilation than other forms of carnitine. [18]

Poor carnitine precursor availability leads to lower carnitine concentrations

Research on pregnant women has repeatedly shown that carnitine concentrations decrease during gestation, even when dietary intake of carnitine *increases*. This was not understood until researchers began studying *precursors*, and they found that low plasma concentrations of GBB were related to the lower plasma concentrations of carnitine.^[19]

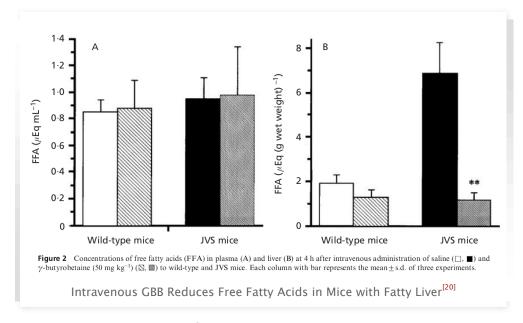
While we never recommend dietary supplement experimentation in pregnant women, and always recommend speaking to a doctor before beginning any new diet or supplementation program, this is very strong evidence that GBB is critically important to overall carnitine levels in normal adults.

Reduces fatty liver in mice

A *very* promising study published in 2010 showed that high intravenous 50 mg/kg doses of GBB (γ-butyrobetaine) reduced liver concentrations of free fatty acids in mice with juvenile

visceral steatosis.[20]

What really impressed the researchers is that GBB can be taken up into the liver and transformed into L-carnitine, [20] and in cases where carnitine transporters are defective, this can make a massive difference!



They conclude with the following:

Consequently, administration of γ -butyrobetaine may be more useful than that of L-carnitine itself for treatment of primary deficiency of carnitine due to a functional defect of the carnitine transporter. [20]

Even though it's an animal model with intravenous use, that's still a powerful conclusion, and worth considering for the appropriate user.

Reduced in people with mood disorders

There's a well-studied connection between the progression of mood disorders and the severity of carnitine deficiency. There's additionally a lot of research showing various forms of L-carnitine supporting these mood disorders.