

Consumer Alert: The NO2/Arginine Scam
by David Barr

The Biggest Scam in Supplement History

Take a look at the history of nutritional supplements and you'll find many scams and cons. It's easy to spot these swindles in hindsight; it's a little tougher to identify them during their market peaks. Well, there's a scam going on right now, a big one. In fact, it's growing even bigger as I write this. Are you falling for it? Are you being suckered by bad science and questionable marketing tactics?

Let's cut to the chase: the biggest scam on the market right now is *arginine blood flow stimulators*. You may know these by the terms "nitric-oxide stimulators" or "NO2 supplements."

Wait, you *already* knew these supplements were worthless? And you think you *already* know what the scam is? Doubtfully. Because I'm about to reveal the *real* con behind these supplements. In this Consumer Alert, I'll not only blow the lid off of the whole scam, but I'll also reveal to you a better hemodilator that's been proven for years to increase blood flow, aid in recovery, and stimulate muscle protein synthesis.

This article covers the science showing why arginine products don't stand up to their claims, but the rabbit hole goes *much* deeper than that. Hang on Alice, you're in for a wild ride.

Why Arginine? Why Now?

Why are so many supplement companies focusing on arginine? Well, now that prohormones are banned, companies are scrambling to throw out the next big supplement to keep them in business. If nothing truly groundbreaking is within their grasp, they'll come out with a worthless supplement supported by dubious science. Want to know what's really pathetic? If this garbage supplement makes some money, other companies will *rip off* the bad idea and market their own versions, regardless of whether or not the supplement works!

Are the copycats and knockoffs, with their additional bells and whistles, better? No. In fact, some sleazy manufacturers are even including potentially harmful substances like [glycocyanine](#) in their products!

This copycat movement was really noticeable at the recent Olympia Expo, where only variations on two products seemed to exist: creatine and nitric oxide stimulators. While readers may be aware of the inherent risks of creatine wannabes from our [Consumer Report on Dangerous Creatine](#), recent evidence demonstrates how nitric oxide stimulators can be considered the greatest con since ENRON. Let's dig into the evidence.

Hemodilators: Theory and Practice

The hemodilator (or blood vessel dilator) products saturating the market are purported to stimulate blood flow and subsequently enhance nutrient delivery to muscles, resulting in increased size and strength. As you may know, these products contain little more than the amino acid arginine, something that's been on the supplement market for years and years. Basically, arginine supplementation is claimed to stimulate the synthesis of the hemodilator nitric oxide (NO) in our blood vessels.

The existing theory looks like this:

Arginine -> Nitric Oxide -> Vasodilation -> Nutrient Delivery -> Muscle Growth and Strength

Now there's nothing inherently wrong with arginine. In fact, it's an important amino acid. It's just not *the* amino acid to really help your gains — more on that later.

New research has been revealed since the first T-Nation article on these types of supplements was published. Now we can focus on that which is directly applicable to us: studies on healthy adults.

Sick Over Arginine

The whole hemodilator theory is relatively simple. Arginine is the precursor for NO synthesis and it's been shown that high dose arginine infusion directly into the bloodstream can lead to vasodilation in healthy fasted humans (17). Unfortunately, high doses can lead to decreases in total body water and sodium (4). And even a dose as low as 10 grams has been associated with gastric upset when consumed orally (26,14).

Researchers involved in a *third* study demonstrating oral arginine-induced GI distress actually had to reduce the quantity originally given so the trials could be completed effectively (29). Despite the reduction to seven grams an hour for three hours (for a 200 pound man), the researchers reported: "All of our subjects reported mild intestinal cramping and diarrhea that lasted for approximately five hours."

But wait, it gets worse! This arginine dose *still* had no significant effect on glycogen storage following exercise (29)! Because oral arginine only has 70% bioavailability, and up to 50% of this can be broken down to ornithine, taking arginine tablets or powder is impractical for research (6, 9). This is why arginine is usually infused directly into the blood via peripheral IV for scientific studies, and even then an impractical dose of 30 grams of this amino acid is common.

In fact, one study compared infusions and oral dosing. The researchers found that six grams of arginine had no effect via either route of administration, while it took a 30 gram

infusion to cause vasodilation (6). So, it takes a 30 gram IV dose to get results. If we were to get these results from an oral dose, we'd have to take 43 grams because only 70% of it is bioavailable (i.e. $30 / .7 = 43$).

Now if 10 grams can cause gastric upset, then the 43 gram oral dose (with bioavailability taken into account) makes me more than a little uneasy.

Arginine: A No Go for NO

If you think that this lack of effect is an isolated incident, other studies investigating high oral doses of arginine and NO induced blood flow have shown no effect when 21 grams (7 g 3x/d) were used (1). Two additional studies where 20 grams per day were taken for 28 days also showed no effects (11,12).

At first, this complete lack of effect was a little surprising considering that arginine is the precursor for nitric oxide synthesis. But upon closer inspection, natural arginine levels are far in excess of what should activate the enzyme responsible for NO production — an effect known as the arginine paradox (21).

In yet another study, a six day, arginine free diet had no effect on nitric oxide synthesis. This indicates that arginine isn't limiting for NO production, and its regulation is far more complicated than supplement companies would have us believe (9).

Of course, the whole rested and fasted thing doesn't apply to you, so let's see what happened when exercise was involved. This next noteworthy study used 10 grams of arginine along with 70 grams of carbohydrates in subjects who either performed resistance training or cycling exercise (26). The results? There were *no changes* in blood flow or glucose uptake compared to placebo, regardless of which mode of exercise was used. This is significant because it directly contradicts the claims of the supplement manufacturers.

For those who are more skeptical, or perhaps just brainwashed by flashy advertising, you're probably not happy with studies using pure arginine. Oh no, it has to be *special* arginine, like the ones used in the popular products, before you'll believe any results. Fine, let's look into the science and crack that nut.

The Acid Test

While it's important to understand the evidence behind normal arginine supplementation, many would argue that it doesn't apply to the original nitric oxide-stimulating supplement, NO2. This is because the aforementioned product contains arginine alpha-ketoglutarate, not simply arginine. The theory is that alpha ketoglutarate (AKG) somehow makes this supplement "work." Okay, that's cool, let's see what science has to say.



This specific product had several studies performed on it, and they were presented at the International Society of Sports Nutrition conference in the summer of 2004. While the findings do not yet come from peer reviewed publications, they yield important information about the efficacy, or lack thereof, of this supplement.

The first study examined the blood levels of arginine and "time released arginine" (following a four gram supplementation with each) to determine whether the latter enhanced the duration of elevated blood arginine levels (18). The reasoning for this study is due to the claim that NO2 has time-release technology, resulting in "perpetual pumps."

Unfortunately for the company, blood arginine levels were nearly all quite similar, and at times *30% lower*, in the time-release trial compared to the pure arginine trial! The reason for the lower levels of the former group remains elusive, but could be due to a decreased absorption by the gut, an increased uptake by tissues, or a half dozen other fates for arginine (see 4). Not surprisingly, there was nothing resembling a "time release" effect.

The second study of interest evaluated the effects of NO2 on body composition, muscle strength and endurance (8). For eight weeks, subjects took either 12 grams of NO2 or placebo and underwent a resistance training protocol. At the end of the time period, subjects between groups had *no differences* in either muscle mass or body fat percentage.

Interestingly, the NO2 group threw an average of 19 pounds onto their bench 1RM, while the placebo group added less than a six pound mean. Does it seem strange to anyone else that this supplement alone supposedly added an average of more than 13 pounds to bench press 1RM over placebo *without* a concomitant change in muscle mass? This would indicate that the changes are strictly neural in origin, which gets quite complicated and goes beyond the scope of this article.

I'll briefly mention that while nitric oxide itself can have a negative effect on the force of muscle contraction (25), this effect has yet to be shown in humans, and doesn't warrant serious consideration for our purposes. More importantly, all of the scientific evidence indicates that it's *not even possible* for us to consume high enough levels of arginine to effectively increase nitric oxide levels! Since this unpublished study is already gracing

the advertisements for this supplement, we need to examine the results in a little more detail.

If the subjects in the above study were untrained, they would all add a significant amount of strength without changes in muscle mass within the first several weeks of working out. In this case, these rapid neural adaptations would be expected in both groups, but wouldn't explain how arginine seemingly tripled the improvement in the nervous system activation.

However, since the subjects *were in fact* trained, the situation is even more puzzling. Unlike novice trainees, strength increases in trained individuals tend to be more a result of muscle growth, which means that there should've been some changes in lean body mass accompanying the other gains. There wasn't.

I would've been impressed, albeit skeptical, by a three or four pound gain over the placebo group on bench press 1RM, but an average of 13 pounds?! Looking at it another way, this means an average gain of two and a half pounds on bench 1RM each week, *and* this progress is maintained for a whole eight weeks on the same program!

If this trend continued for all exercises, which it presumably does, everyone with these results could easily become a competitive powerlifter. Although such improvements might be theoretically possible, you must remember that these fantastic results were achieved on a training program and diet that normally leads to a mere six pound addition to bench press. Furthermore, to have such incredible strength gains throughout every muscle group, without even the *slightest* trend for improved muscle growth, demands questioning.

Considering the other research which showed no effect on blood flow and no time release effect, the results just don't fit. Whether it be improper group selection, outliers in the data, or measurement error, the results presented remain questionable.

With my objective experience as a strength coach, researcher and bodybuilder, I don't believe these results to be possible. Having said that, this article is merely intended to give you the facts that you won't get anywhere else, and allow you make up your own mind.

Let's sum of the results of this study and others:

- **One group used oral arginine in this study, *but*** oral arginine supplementation doesn't affect blood flow.
- The arginine group used "time release" arginine, *but* so-called time release arginine is not actually time released.
- The trained individuals in the NO2 group got stronger without increasing muscle growth, *but* trained individuals get stronger mostly due to muscle growth.

- The training program and diet alone yielded a six pound increase in bench 1RM, *yet* four grams of NO₂ taken three times a day tripled strength gains on the same program.

In short, something just isn't right.

But Wait, I Thought I Felt Something!

I'm sure some people are reading this and thinking, "But I *know* these products work because I've taken them and *feel* their effects!" While these perceived effects are potent, I submit to you that based on the scientific evidence, this is merely a result of the placebo effect.

The placebo effect is when someone uses an inert substance, which should produce no effect, yet somehow still experiences an effect. This occurs frequently when pharmaceutical companies test a new drug. They give one group the real drug and another group an inert sugar pill. Interestingly, the group receiving the sugar pill often has a series of side effects like dry mouth, headaches, dizziness, adding ten pounds to their bench, etc. — all caused by their own minds!

One famous research analysis calculated the placebo effect to account for 75% of a drug's effect, although this exact figure remains controversial (19). It's amazing what dogma we can succumb to in the face of contrary reason and evidence, merely because we *want* to believe something. This belief, desire and trust all seem to work at the neurological level of the brain (10). This indicates that it's more than a matter of a few people being tricked by unscrupulous companies.

Unfortunately, the situation is even worse when it comes to sports supplements because of our *expectations*. Hundreds of advertisements with spectacular claims, combined with our incredibly strong desire to believe that these supplements work, often defeat our poor psyches. I call this a *directed placebo effect*, because we have not only a simple belief in what the supplement is supposed to do, but a powerful desire to believe in its effectiveness.

What can make our desire to believe in these products even stronger is the very fact that we've already purchased them! After all, recognizing that a product doesn't work is like admitting that we were duped — something no one wants to do. Hey, I've fallen into this trap too in the past. We're all susceptible.

Even if you still believe in the products in question, you'll now be aware of this powerful psychological effect.

But What About Growth Hormone Release?

In response to this rather damning article, some companies will scrounge up data showing that arginine can elevate growth hormone levels. While we've known for the past decade that this applies only to *huge* doses infused into the bloodstream, many people will be unaware of this trick.

Now, there's evidence that ingesting 22 grams per day (in a 200 pound man) of arginine aspartate increased nocturnal growth hormone output (5). The peak GH output during sleep was increased by an average of 60%. Unfortunately, only five subjects were studied and one of them had *four times* the peak output of the others. Without that one oddball subject, the average peak was cut in half! (Again, these are just peak measurements, not total levels.)

Also of note, prolactin increased by an average of 75%. This hormone is associated with decreased Testosterone (7)! What's really scary is that a mere five grams of arginine consumed during exercise actually *decreased* the resistance exercise-induced increase in GH output (24)!

The bottom line is that you can forget about arginine and GH stimulation, despite what the advertisements try to tell you.

The Real Secret

Here's where things get *real* interesting. You may want to be seated for this, because I'm about to blow the lid off the whole deal.

Arginine is the amino acid known to be the most potent insulin secretagogue, meaning that it causes insulin release from the pancreas (4). Now this is of critical importance, because *insulin itself stimulates vasodilation and blood flow* (2), and this occurs via elevations in nitric oxide synthesis (27).

So arginine stimulates insulin, and insulin stimulates nitric oxide. Nitric oxide causes vasodilation and increased blood flow. Hmm... Combining this info with what the scientific literature tells us, we can see that much of arginine's vasodilatory effect can be attributed to *insulin secretion*!

In fact, one study examined the extent of this very effect, and the results are shocking. Researchers infused the standard 30 grams of arginine with or without blocking insulin release from the pancreas (15). As usual, the massive arginine infusion increased blood flow. But, when insulin release was blocked, blood flow decreased by 77%!

When the latter experiment was repeated with an insulin infusion, blood flow was completely restored! So, over three-quarters of the increased blood flow response was caused by insulin. While not all arginine-induced blood flow can be attributed to insulin, you must remember that these studies use the equivalent of over 40 grams orally ingested arginine, which isn't even possible to tolerate.

The Revised Theory:

Arginine -> Insulin -> Nitric Oxide -> Vasodilation -> Nutrient Delivery -> Muscle Growth and Strength

You have to wonder if the companies who produce these supplements knew this when they began to market them. If they did, then they intentionally swindled people. If they didn't, then they clearly didn't have any idea what they were asking people to put into their bodies. Either way, it's lose-lose for them.

To make things worse, AKG is being shown to play a role in stimulating insulin secretion (23), suggesting that companies may have indeed been trying to pull the wool over our eyes the whole time.

While this addition may seem beneficial, you have to remember that we still have no real evidence even *suggesting* that any of these products work at reasonable doses. And don't forget, an increase in insulin levels (and therefore blood flow) is all too easy to obtain without NO products.

Why would we use arginine to stimulate blood flow when we can get *direct* effects by manipulating insulin? In Part II of this article, I'll tell you how to do that without arginine supplements. The good news is, you're probably already doing it!

Summary

- Arginine blood flow stimulators ("nitric-oxide" or "NO₂" supplements) have been shown to increase vasodilation, but only in unfed people receiving enormous doses through an IV.
- Oral arginine supplementation doesn't affect blood flow.
- A dose as low as 10 grams has been associated with gastric upset when consumed orally. This dose has no significant effect on glycogen storage, even if it didn't cause diarrhea.
- Time release arginine is supposed to lead to a "perpetual pump" effect. New studies have shown this not to be the case.
- NO₂ was shown to have no effect compared to a placebo on body composition or muscle strength.
- It's not possible for us to consume high enough levels of arginine to effectively increase nitric oxide levels.

- Copycat NO2 products are no better than the original supplement. In fact, those that contain glycoyamine should be avoided because of potential health concerns.
- If you think these products work for you, then you'd better look into the placebo effect.
- Arginine might temporarily elevate growth hormone levels, but only if you're able to take unrealistic doses. There's little evidence to support that this short term increase in GH would do anything for your physique anyway.
- In one study, arginine aspartate was shown to increase prolactin by an average of 75%. Prolactin is associated with decreased Testosterone levels.
- Five grams of arginine consumed during resistance exercise was shown to *decrease* normal exercise-induced GH output.
- The positive benefits of oral arginine supplementation can only be achieved through doses higher than the human body can handle. And most (but not all) of this effect is mediated by insulin. So if you want to have blood flow increases equivalent to a huge IV arginine infusion, just manipulate insulin through other means (which will be discussed in the next article.)

About the Author

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