

Molecular Hydrogen – Is It the Best Antioxidant You Can Take?

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STORY AT-A-GLANCE

- › Molecular hydrogen (H₂ gas) is a potent selective antioxidant, which means it will not eliminate free radicals to the point of causing an imbalance
- › The H₂ molecule is the smallest in the universe, which allows it to diffuse through all cell membranes, including the blood-brain barrier and subcellular compartments, into the mitochondria. It also has no charge or polarity. All of this gives it superior bioavailability
- › H₂ readily reacts with the toxic hydroxyl radical – the most reactive and oxidative radical in the body – turning it into harmless water
- › H₂ may be very helpful in cases of heart attack or stroke, protecting against the oxidative damage from hydroxyl radicals that occur during reperfusion
- › Hydrogen also helps moderate autophagy, mTOR and IgF1, raising them if needed or lowering them when excessive

This article was previously published July 19, 2020, and has been updated with new information.

Tyler W. LeBaron, founder of the science-based nonprofit Molecular Hydrogen Institute, is one of the most knowledgeable people about molecular hydrogen and its benefits. There are so many benefits we can learn from him and many other researchers from Universities around the world. For starters, H₂ is a potent selective antioxidant. This is

important, as many other antioxidants, such as vitamin C and E are not selective, and when taken in excess, can be counterproductive.

Hydrogen doesn't have that downside, which is one of the reasons why it's one of my favorites. Now, when we talk about molecular hydrogen, we are talking about the gas, the H₂ molecule, which is two hydrogen atoms bound together.

The H₂ molecule is the smallest in the universe, which allows it to diffuse through all cell membranes, including the blood-brain barrier and subcellular compartments, and into the mitochondria. It doesn't need any transporter protein.

It also has no charge or polarity. As explained by LeBaron, that's critical, because charged molecules cannot easily penetrate cell membranes. Charged molecules must go through a protein channel. All of this gives it superior cellular bioavailability.

Health Benefits of H₂

Among the many health benefits of H₂ is its ability to decrease excessive oxidative stress, inflammation and perturbations from normal homeostasis. The key word here is "excess," because some oxidative stress and some free radicals are actually beneficial. For example, you metabolize food through the process of oxidation, and that oxidation is necessary for life to exist.

So, what we're looking for in terms of health is the ability to inhibit excessive oxidative stress and damage. LeBaron reviews this in greater detail in the interview so, for more information, please listen to it in its entirety, or read through the transcript.

As just one example, certain therapies such as photobiomodulation, exercise and sauna bathing mildly increase oxidation in the body, and that oxidation is what induces various beneficial effects such as the induction of heat shock proteins (HSP). This process is known as hormesis.

"This is an important word ... when we talk about the benefits of molecular hydrogen because it seems to work through some similar processes of

hormesis," LeBaron says.

H₂ Is a Selective Antioxidant

When it comes to oxidative stress, all you really want is a return to homeostasis. You don't want to neutralize all free radicals. Many antioxidants have a high number of electrons that can easily and indiscriminately scavenge, react with and neutralize a wide range of radicals or oxidants. Molecular hydrogen, on the other hand, is selective, and thus only eliminates the excess, so that homeostasis is restored.

"Sometimes antioxidants can even exacerbate oxidative stress because they can increase Fenton reaction cycles and redox cycling, and end up being potent pro-oxidants. So, it is very complicated, and we have to be very cautious,"

LeBaron says, adding:

"One of the reasons we know H₂ [is] safe is because it simply does not have the reductive power or potential to neutralize or react with some of these critical important signaling oxidants, such as hydrogen peroxide, superoxide radicals and nitric oxide. It just does not have the ability to react with these, even in vitro. If you just put the two together, they don't react."

On the other hand, H₂ readily reacts with the toxic hydroxyl radical – the most reactive and oxidative radical in the body – turning it into harmless water. Studies suggest H₂ may be very helpful in cases of heart attack or stroke, for example, protecting against the oxidative damage from hydroxyl radicals that occur during reperfusion.¹ In my view, molecular hydrogen should be implemented ASAP in all cases of heart attack and stroke for this reason.

There's no risk, it's very inexpensive and the upside potential is enormous. LeBaron cites animal research published in the Journal of the American Heart Association² showing H₂ administration increased the post-cardiac arrest syndrome survival rate from 43% in the control group to 92% in the H₂ group. When combined with therapeutic hypothermia,

which inhibits the creation of free radicals, the survival rate shot up to 100%. It simply doesn't get any better than that.

“ H₂ readily reacts with the toxic hydroxyl radical — the most reactive and oxidative radical in the body — turning it into harmless water. H₂ may be very helpful in cases of heart attack or stroke, protecting against the oxidative damage from hydroxyl radicals that occur during reperfusion. ”

According to LeBaron, the Japanese government has now approved the inhalation of H₂ gas as an advanced medicine for the treatment of post-cardiac arrest syndrome.³ He also reviews some of the studies that are currently underway to investigate the benefits of molecular hydrogen inhalation during heart surgery and other instances.

H₂ Is a Signal Modulator

Aside from being a selective antioxidant, H₂ acts as a gaseous-signal modulator, and thus is able to influence gene expression and protein phosphorylation cascades involved in signal transduction, all of which help explain its therapeutic effects. One of the primary pathways that H₂ activates is the Nrf2 pathway. LeBaron explains:

"The Nrf2 is this protein that's bound to another protein, Keap1, and when there's an assault of oxidative stress, those two separate. Then the Nrf2 is able to diffuse into the nucleus of the DNA. It binds to the electrophile response or ARE, the antioxidant response element, portion of the DNA.

When it does that, that ends up leading to the production of a whole bunch of endogenous antioxidants like glutathione, superoxide dismutase and catalase ... When we talk about antioxidation and detoxification, a lot of that is regulated and controlled by Nrf2. That is the master regulator. So, it is a key protein

involved in many processes [and] hydrogen gas is able to activate the Nrf2 pathway."

Importantly, though, contrary to other Nrf2 activators, H₂ only activates Nrf2 if it's actually needed. In this way, the risk of it suppressing beneficial free radicals like nitric oxide is minimized. Indeed, H₂ appears to be one of the safest therapeutic options available. Its downside potential is almost nonexistent.

"It tends to bring things back to homeostasis," LeBaron says. "The further something is away from homeostasis, the higher the probability that hydrogen gas will be able to help bring that back into homeostasis. If something is already at a perfect level, well, then, you may see that hydrogen gas didn't do anything ..."

Again, hydrogen gas has this dual role where it can both protect against the oxidative stress, as well as act as this mild hormetic effector in the mitochondria to increase mild amounts of free radicals, similar to an easy bout of exercise for example, which can then induce these protective effects."

How to Administer H₂

The easiest way to get hydrogen gas into your system is to dissolve a molecular hydrogen tablet in water and drink it. In the interview, LeBaron warns us why we need to be skeptical and cautious about electrolysis machines, as they often don't produce anywhere near the concentrations required. In clinical studies this is often 1.6 mg/L and above, which at first doesn't sound like very much, but it is significant as LeBaron further explains:

"There are a couple of things to consider when you drink hydrogen gas. No. 1, 1.6 mg/L as a solubility doesn't sound like very much ... [but remember] that hydrogen gas is the smallest molecule in the universe. Of course, 1.6 mg doesn't weigh very much because it's hydrogen gas ... but it's actually a lot of"

molecules. In fact, there are more molecules in 1.6 mg of hydrogen than there are molecules of vitamin C in a 100-mg dose.

You have to compare molecules to molecules or moles to moles, not just weight to weight. What weighs more, a pound of gold or a pound of feathers? Right? They weigh the same ... So, when we look at molecular hydrogen, there is actually quite a bit.

Now, get this. When you inhale, say, a 3% hydrogen gas, then that's going to increase the cellular concentration to a certain level. That exact same level, if we can calculate it based on Henry's law and the dose you're ingesting from drinking hydrogen water, that concentration in the cell can also be reached by just drinking hydrogen water.

Because if you drink all of it at once ... [it] immediately increases the cellular concentration to the same level that you would get if you were inhaling hydrogen gas at 2% or 3% level ... You're also able to enact various second messenger systems that maybe you're not getting with inhalation."

Research has shown H₂ water can improve nonalcoholic fatty liver disease⁴ and metabolic syndrome,⁵ both of which are diet-driven conditions. In a recent study⁶ looking at metabolic syndrome, a high dose of H₂ was used using hydrogen-producing tablets.

The study involved 60 subjects and lasted for six months and "significantly reduced blood cholesterol and glucose levels, attenuated serum hemoglobin A-1c, and improved biomarkers of inflammation and redox homeostasis." It even "tended to promote a mild reduction in body mass index and hip-to-waist ratio," the study authors added.

"It appears we had some very prominent effects, and even more effective compared to the previous studies leading to this trend that at least in some cases, a higher dose or a higher concentration of hydrogen is more effective than the lower dose, lower concentrations," LeBaron says.

Concentration and Frequency Matter

Aside from making sure the concentration is sufficiently high, you also want to pulse your intake, as the more continuous the exposure, the less effective it is. LeBaron further explains:

"Let's say [you take] 6 mg of hydrogen and you're going to take all 6 mg evenly in a 24-hour period. That means you're essentially sipping on hydrogen water throughout the day.

If you do that, you may not get as good of benefits because you're not getting a high enough dose of hydrogen in the body in order to reach the cellular concentrations required to induce those changes at the cellular level that you need.

Now, if in contrast, if you were to just take the full 6 mg all at once, that is probably going to be more effective than taking it throughout the entire day. So, I will say if you are going to get hydrogen and try to get the benefits, then you would want to get as high of a dose you can all at once, and then you could probably do that multiple times a day.

I don't know if it's better to take 6 mg or 10 mg of hydrogen once a day or six times a day. Maybe the six or 10 times a day is going to be more effective, or just as effective, because you're still getting spikes. But then again maybe not."

Clearly, the studies need to be done to determine the best frequency, but until then, it would seem that customizing the dose to your personal circumstances might be more appropriate. So, if you're in normal, nonstressful circumstances at home, not exercising much at all, then maybe once day is sufficient.

On the other hand, if you exercise vigorously then it might be more appropriate to take it a couple of times a day. If you travel by airplane, taking it every two hours while flying might be appropriate. The good news is, H₂ is quite safe, so you're unlikely to do harm.

Another benefit when using hydrogen tablets is that they contain highly bioavailable unbound magnesium ions. Each tablet will provide about 80 mg of ionic magnesium,

which is about 20% of the RDA.

Synergistic Effects With Other Therapies

H₂ gas can also be used together with other supplements and therapies for a potential synergistic effect. For example, you can take it along with a sauna, both of which produce heat shock proteins, or with nutritional ketosis or exogenous ketones. Another example is hyperbaric oxygen therapy.

"When it comes to the sauna, I think that's great," LeBaron says. "I probably would do the hydrogen before anything ... Again, [we're] talking about this preconditioning hydrogen effect.

If I can just back up and talk about one study that I think helps at this stage, about NAD⁺ and NADH. These are very important molecules. The higher the ratio of the NAD⁺ to NADH, the better ... In this interesting study,⁷ they used a toxin in a cell culture, and as would be expected, that NAD⁺ to NADH ratio decreased, and that ends up causing all of these pathological problems and cell death.

When they administered the hydrogen gas, it helped maintain those levels up higher. Now, this is part of the issue: For part of the study, they just did it in cell cultures, so you can imagine this little Petri dish, and you add hydrogen gas in there.

Well, that hydrogen gas will only be in there for 20 minutes, half an hour or 40 minutes, depending on the concentration. It's not going to be there for very long. They found there was a therapeutic protective effect against that toxin for about 24 hours. It maintained that effect ...

Then there was a clinical study on rheumatoid arthritis⁸ where they used high-dose hydrogen water for four weeks. After four weeks, there was still a protective effect of molecular hydrogen. There were still decreases in the disease rating score and oxidative stress. So, it really had an effect on gene

expression, epigenetics and signal modulation. Much more is going on here than just a radical scavenging activity.

Taking these together, when we look at other things such as the sauna, the sauna really is quite a mild thing ... [but] I still like the idea of taking the hydrogen before. When you're talking about hyperbaric oxygen, then I think there's even more rationale of taking the molecular hydrogen [30 to 60 minutes] before as a pretreatment, preconditioning ...

Ketones, whether they're endogenous or exogenous, are very beneficial for the mitochondria, as long as the mitochondria are ready for them. Ketones can also increase free radicals, at least initially, but this is also what's very good, because in the long run they can decrease oxidative stress. Part of this is why you can upregulate the Nrf2 pathway.

Well, hydrogen gas being able to both suppress excessive oxidative damage as well as improve and activate the function of the mitochondria, improving the mitochondrial resting membrane potential, it will have influence in the mitochondria transition pore, so you don't have pathological problems ...

So, there are some areas where ketones seem to work, as does hydrogen gas ... Hydrogen [can also] induce and actually enhance autophagy^{9,10}... By so doing, you're going to get therapeutic protective effects from the hydrogen gas. However, there are other studies showing that hydrogen gas inhibits excessive autophagy.^{11,12}

So, that's how cells die, right? You have necrosis, you have apoptosis, and you have autophagic cell death. When you have too much going on – and a lot of drugs or interventions can potentially cause an excessive amount of autophagy – then that's bad. Hydrogen gas ... was able to prevent the excessive amount of autophagy being produced."

Similarly, H₂ gas can both increase and decrease mTOR activation,^{13,14} depending on what your body needs. Ditto for IgF1.^{15,16} What this means is that if you're fasting or

doing time-restricted eating, which activates autophagy, taking molecular hydrogen not only can optimize autophagy, but also lower it if too much is taking place. That could make long-term fasting much safer. What's more:

"When you take hydrogen, you increase gastric ghrelin secretion.¹⁷ Ghrelin is the hunger hormone. One of the first things [that happens] when you fast is you increase ghrelin. Ghrelin is extremely neuroprotective and anti-inflammatory and has a whole bunch of benefits.¹⁸

Well, hydrogen also increases ghrelin. So, in a lot of ways, hydrogen mimics fasting from autophagy to ghrelin, to a lot of other pathways that are activated, but it depends on the condition."¹⁹

Dosing Basics

The normal dose is one tablet – which is considered an appropriately high dose – in 500 mL or 16 ounces of water. That will give you a concentration of about 10 mg of H₂ per liter (10 mg/L), which means you're getting a dose of 5 mg. As soon as the tablet has dissolved, you'll want to drink the whole glass before the cloud of H₂ gas dissipates.

The rate at which it dissolves can vary from anywhere from one to two or three minutes, depending on how cold the water is. If you put it in iced water, it's going to take even longer. Ideally, use room temperature water, as the colder it is, the longer it takes for the tablet to dissolve, and the longer it takes, the less of the gas will remain by the time the tablet is fully dissolved.

Also, use still water, not sparkling water, which has CO₂ dissolved in it, as that will disperse the H₂ gas out faster. You want to drink it quickly while it still has that milky look. The white cloudiness is the suspended hydrogen. If you wait until the water turns clear, the hydrogen gas has evaporated away. Again, if your body is under serious stress, you may take four or five tablets a day. If not, a single tablet a day would probably be sufficient.

For more information about molecular hydrogen research, visit the National Institutes of Health library²⁰ and search for molecular hydrogen. Also be sure to check out the [Molecular Hydrogen Institute's website](#).

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