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Why Molecular Hydrogen Is a Superior Antioxidant

Analysis by Dr. Joseph Mercola ✔ Fact Checked | March 19, 2023

STORY AT-A-GLANCE

- Molecular hydrogen acts as a selective antioxidant, meaning it doesn't indiscriminately suppress free radicals
- It uses your body's biological systems and feedback loops to identify where and when you're under oxidative stress, and when found, pathways are activated and key proteins released that cause your DNA to make the antioxidants themselves
- Molecular hydrogen is not intrinsically an antioxidant. Rather, it helps your body make its own endogenous antioxidants. This is what makes molecular hydrogen so unique
- Molecular hydrogen has been shown to have therapeutic benefits in more than 170 different animal disease models
- The reason it has such diverse benefits in so many different disease models is because all of them have excessive oxidative stress, redox dysregulation and inflammation as their root cause. By regulating the oxidative pathways, molecular hydrogen is able to address these root causes

In this interview, repeat guest Tyler LeBaron, MSc., Ph.D., reviews some of the many benefits of molecular hydrogen (H_2). Perhaps most importantly, molecular hydrogen acts as a selective antioxidant, meaning it doesn't indiscriminately suppress free radicals.

It uses your body's own biological systems and feedback loops to identify where and when you're under oxidative stress, and when found, antioxidant genes are stimulated

and key antioxidants are transcribed from your DNA. So, molecular hydrogen is not in and of itself a direct radical-scavenging antioxidant. Rather, it helps your body make its own endogenous antioxidants. This is what makes molecular hydrogen so unique.

This is crucial because excessive antioxidants use can be deleterious and molecular hydrogen serves as a redox regulator, so, just like Goldilocks, you get just the right amount, not too much and not too little, which makes your cells very happy.

H_2 Activates Nrf2 Pathway

One of the pathways activated by H_2 when free radicals are present is the Nrf2 pathway. LeBaron explains:

> *"In your cell you have this protein, Nrf2, and it's attached to Keap1. They're always attached together. But when you get oxidative stress … it can cleave off.*
>
> *[Oxidative stress] causes the cleaving off of the Nrf2 and the Keap1, and the Nrf2 can then diffuse into the nucleus [where] it binds to the ARE, the antioxidant response element of the DNA. [This triggers] the production of all these endogenous antioxidants — Phase 2 enzymes of detoxification and antioxidation — and there are over 200 of them."*

This is one of the primary benefits of **molecular hydrogen**. It's also what makes molecular hydrogen so useful for such a wide variety of conditions. According to LeBaron, it's been shown to have therapeutic benefits in more than 170 different animal disease models.

> *"What this means is, for example, there are lots of ways to induce diabetes in an animal model. Using these different models, we can show molecular hydrogen has therapeutic effects. And, yes, the Nrf2 in some cases seems to be extremely important. In fact, by using gene knockout or or interfering RNA, you can blunt the benefits of molecular hydrogen. So, the Nrf2 is very important,"* LeBaron says.

Molecular Hydrogen Is an Important Nrf2 Regulator

Sulforaphane, found in broccoli, is another well-studied Nrf2 activator. But in contrast to sulforaphane (as well as other Nrf2 activators), molecular hydrogen does not disturb redox homeostasis within the cell by adding too many antioxidants.

Redox homeostasis is when there's a specific balance between reducing and oxidizing reactions within the cell. Homeostasis is what you need for optimal cellular health, and either too many free radicals or too many antioxidants can have detrimental effects. When you add molecular hydrogen to a cell that is already at redox homeostasis, however, there's no increase in Nrf2 or other proteins, so it doesn't accidentally push it out of homeostasis. As explained by LeBaron:

> *"That's important because we don't want to have reductive stress. If you were to induce the Nrf2 pathway indiscriminately and just keep it going, that would be reductive stress and that would be problematic.*
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> *In fact, there are genetic mutations where the Nrf2 is hyperactivated, and that leads to all sorts of problems. Cancer sometimes can activate the Nrf2 really strongly … So what we really are talking about is the regulation of Nrf2.*
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> *When we administer molecular hydrogen to healthy cells, we don't see changes in the Nrf2 level at the protein level. However, if we were to administer a toxin or some other stress, that's when we would see that molecular hydrogen was able to induce the Nrf2 — and many other proteins, not just the Nrf2 — and provide a protective effect.*
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> *That is different than anything else out there. And it has this pretreatment effect as well. So, for example, in one study, they administered molecular hydrogen into a cell culture, and after that, they administered a common environmental toxin.*
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> *The exposure caused a decrease in the antioxidant status. So, you could see markers of increased oxidative stress, you could see decrease in superoxide*

dismutase levels, all these important antioxidants, as well as a decrease in NAD+ to NADH ratio. Having a high ratio is very important, and this stress caused a reduction in this ratio.

However, in the cells that were pretreated with molecular hydrogen, it prevented those reductions from happening, and it provided a protective effect for 24 hours even after the hydrogen gas was out of the cell culture and there was no molecular hydrogen left. That's because molecular hydrogen works at the gene level, epigenetically even, modulating proteins, the signaling pathways and the phosphorylation cascades …

So, we're not just activating Nrf2. We're regulating its production so it's not too high, not too low … [Molecular hydrogen is an] adaptogenic redox regulator, basically …

And, we are able to provide a protective effect for, say, 24 hours in this case, as opposed to only when it's present. It's amazing to think that molecular hydrogen is able to change how the genes express themselves so that it's going to have favorable effects even after it's out of the body."

Considerations When Administering Molecular Hydrogen

While there's no risk of overdosing on molecular hydrogen, intermittent exposure produces the best results. It's also important to get the optimal concentration of H_2 molecules to your cells, at least a concentration of about 10 micromolar or higher at the cellular level.

Dose-dependent benefits are seen between 10 micromolar all the way up to 800 micromolar, which is considered the saturation level of molecular hydrogen in water at sea level. The therapeutic dose of regular hydrogen water is 0.5 milligrams per liter (mg/L). Saturation is reached at 1.57 mg/L, but some technologies such as tablets can give much higher levels.

So, when we talk about the "right" and "wrong" ways to take molecular hydrogen, it has to do with the concentration of H_2 that you're getting. For example, the "wrong" way to drink H_2 water might be to take a few sips every few minutes, finishing it in an hour.

With each passing minute, the H_2 concentration reduces, leaving you with next to nothing by the time you're finished. You also won't get that approximate 10 micromolar level concentration required to transcribe the DNA to produce your endogenous antioxidants.

When using molecular hydrogen tablets, which is my preferred method, the nanobubbles contain hydrogen gas, so once the bubbles are gone, you've lost most of the hydrogen. So, to ensure maximum concentration, you have to drink it as soon as the tablet has dissolved and the water is still cloudy-looking.

Hydrogen is the smallest-known molecule in the universe and it has no electrical charge, so it can easily penetrate any cell membrane once in your body. However, it will follow a concentration gradient, so when you drink hydrogen water, it'll go to the stomach first, followed by the intestines and liver before entering your systemic circulation.

> *"Through Brownian motion and this diffusion gradient, it'll be a passive diffusion, simple diffusion into the cells, where it's going to induce effects,"* LeBaron says.
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> *"So going back to the tablets, the concentration of the hydrogen in the tablets is not just in dissolved form, but it's in this quasi-suspended, micro-macro nano bubble form that has a lot of hydrogen density, so to speak, in the water.*
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> *So, it's not going to be as stable. So, absolutely, in that case, you've got to drink it very, very quickly while it's still cloudy. Otherwise, you're going to lose a high percentage of the hydrogen …*
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> *Unfortunately, some hydrogen products do not reach that threshold of 0.5 mg/L. But with the tablets, because so much [hydrogen] is dissolved and a lot of that is in the suspended or quasi form, you have a very high volume of molecular*

hydrogen, which requires you to drink it faster, but you can get these higher doses of molecular hydrogen."

What to Look for When Buying Molecular Hydrogen

When it comes to buying a high-quality H_2 product, make sure it's certified according to the International Hydrogen Standards Association (IHSA). This is your assurance that the product is truly capable of at least delivering the proper amount of molecular hydrogen. LeBaron explains:

*"We **published a paper** showing how ORP [oxidation-reduction potential] is very inaccurate, especially if the pH is anything but neutral. So, with the tablets, you might measure something like 0.5 mg/L when really it's 5 mg/L because of the pH. So, we really can't use ORP-type meters or other methods.*

It has to be gas chromatography. And IHSA uses the gold standard, gas chromatography, and then does a series of testing for safety and purity and a number of other things in order to be classified as a product that could be recommended and used in clinical studies."

In the interview, LeBaron also does a quick review on the ideal dosing when using inhaled hydrogen. I've limited my summary to hydrogen water here, as this is the easiest way to get it, and in many cases, drinking hydrogen water is more effective than inhalation. Molecular tablets are also ideal when traveling, as you can simply drop one in a glass of water.

"In certain cases, it's 100 times more effective, just looking at different protein expressions, for example," LeBaron says. *"But in other scenarios, the inhalation might be able to work on different pathways, different areas that the drinking cannot, and so they don't really compete with each other and there could be an additive or synergistic benefit from them.*

In the past, I would say most of the research has been done on drinking hydrogen water in clinical studies, and that's still probably the case, but there

are more and more clinical studies being done now with the inhalation of molecular hydrogen that are showing favorable effects."

Molecular Hydrogen Protects Against Radiation Damage

One of the benefits of molecular hydrogen is that it helps protect against radiation damage, including X-rays from medical diagnostics and the gamma rays you're exposed to during flights. Every time I fly, I take it just before takeoff, as it takes about an hour before the ARE enzymes are activated and you start producing endogenous antioxidants.

Then I take it once every hour for as long as I'm in the air. If you're using tablets, put one tablet in 16 ounces of room temperature water and drink it as soon as it's dissolved. Cold water will make the tablet dissolve slower, so you'll lose some H_2 while waiting for it to fully dissolve. Don't use carbonated water as the carbon dioxide gas will lower the concentration of hydrogen gas that you can have in the water.

Alternatively, you could pretreat yourself by taking molecular hydrogen for two or three days beforehand. That way, by the time you're exposed to the radiation, you'll already have a level of built-in protection. If you need a CT scan, consider pretreating yourself for a couple of days and then take another dose about 30 minutes or so directly before the test.

Molecular Hydrogen Helps Ward Off EMF Damage

Molecular hydrogen may also help ward off some of the damage incurred by nonionizing electromagnetic fields (EMF). One theory advanced by Martin Pall, Ph.D., is that the primary danger of EMFs is the mitochondrial damage triggered by peroxynitrites, one of the most damaging types of reactive nitrogen species.

Low-frequency microwave radiation activates the voltage-gated calcium channels (VGCCs) in the outer membrane of your cells, causing them to open, thus allowing an

abnormal influx of calcium ions. This activates nitric oxide, which is a precursor for peroxynitrite.[1]

> **“What we need to do is decrease the excessive production of superoxide or nitric oxide. Then we could essentially prevent peroxynitrite formation. And that's exactly what molecular hydrogen does. ~ Tyler LeBaron, MSc, Ph.D.”**

These potent reactive nitrogen species are associated with an increased level of systemic inflammation and mitochondrial dysfunction and are thought to be a root cause for many of today's chronic diseases.

Clearly, limiting your EMF exposure should be your primary strategy, but if for whatever reason you cannot, then you may want to consider taking molecular hydrogen regularly to increase your endogenous antioxidants and limit the damage from peroxynitrite and other oxidative stressors. How does this work? LeBaron explains:

> *"One of the first studies, published in Nature Medicine in 2007[2] … found that in addition to [molecular hydrogen's] ability to reduce hydroxyl radicals, [it could] reduce peroxynitrite. We see a reduction of the peroxynitrite levels, and we also see reductions — like in animals and tissue samples — of nitrotyrosine levels, which is a marker of the peroxynitrite as well.*
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> *Now, calcium signals can induce nitric oxide and activate various NOX enzymes to increase superoxide production, and then you have superoxide and nitric oxide, and they react instantaneously. If they come in contact with each other, they will form peroxynitrite. The only thing that limits how fast they react is the rate of diffusion.*
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> *So, what we need to do is … decrease the excessive production of superoxide or nitric oxide. Then we could essentially prevent peroxynitrite formation. And*

that's exactly what molecular hydrogen does.

This is really fascinating because if you took other antioxidants and you put them in the presence of nitric oxide or superoxide, you could scavenge them. They would donate their electrons and neutralize them. That can be good, but it can also be bad, because your body makes and specifically uses things like superoxide to increase mitochondrial biogenesis, or nitric oxide for vasodilation.

So, we don't want to just neutralize all of these. Hydrogen [is] selective, and if you put molecular hydrogen in the presence of superoxide or nitric oxide, there is no reaction. They don't have a strong enough oxidizing power for hydrogen to react, so we don't have to worry about that happening.

The question then is, how does hydrogen help with the superoxide and the nitric oxide when their levels are in excess production? That goes to this signal modulating effect. With superoxide, typically that's from NADPH oxidase or NOX enzymes that can become hyperactivated.

Molecular hydrogen has this ability to down-regulate this NOX enzyme, so you end up producing less superoxide in the first place. And, if you have less superoxide, then you're going to make less peroxynitrite.

And then, on the other side, when you have nitric oxide production, you have three main isozymes or enzymes. You have the neuronal nitric oxide synthase (nNOS), endothelial nitric oxide synthase (eNOS) and the inducible nitric oxide synthase (iNOS). eNOS, that's in the endothelial cells, so typically, that's good. You want more of that, you kind of lose that as you get older.

Incidentally enough, on a side note, molecular hydrogen can actually improve eNOS. So, we can have better blood perfusion and things in this way.

But the iNOS, specifically from macrophages, can be problematic. And hydrogen has this ability to down-regulate the activity of iNOS, of making this excessive

nitric oxide production. So now you're decreasing superoxide and nitric oxide levels, and consequently you get less peroxynitrite."

How Molecular Hydrogen Can Optimize Exercise Performance

Molecular hydrogen can also be used to boost exercise endurance. LeBaron **published a paper on this in the Canadian Journal of Physiology and Pharmacology a few years ago**. There are also several others, including a systematic review and meta-analysis, that detail its favorable effects. As explained by LeBaron, it can help you push yourself harder, improve blood flow and reduce fatigue.

*"One of the **earliest studies** found [molecular hydrogen could] prevent fatigue during a maximal isokinetic knee extension exercise. Isokinetic just means same speed, so you're on a machine and you're just doing these leg extensions. I think they did 50 in a row, and you just do them as hard as you can.*

The group that took molecular hydrogen was able to maintain a higher force output during those 50 maximal isokinetic knee extensions. Also, they looked at exercising at around 70% your VO2 max, which is about close 70% of your max heart rate, and those who were doing this were able to exercise longer [and] had lower levels of lactate …

One interpretation is that molecular hydrogen may have improved the function of the mitochondria … Now, if we're getting our ATP production from the mitochondria using aerobic respiration, then we don't have to go through the anaerobic pathway of making lactate.

So that's … why we're seeing lactate decrease; we're able to use the mitochondria to make ATP, so now we can exercise better, longer and have less fatigue, especially the perceived exertion.

There are also explanations in terms of lactate clearance and accelerating the Cori cycle and different things. But mitochondrial bioenergetics are probably a major target of molecular hydrogen …

[It's also] protective, because when you exercise, you breathe a lot more and that's going to make more free radicals. A lot of those free radicals are going to be very good for your body because it's going to force you to make more antioxidants, it's going to increase mitochondrial bioenergetics and all this stuff, but you're still causing damage.

You're still damaging DNA. With molecular hydrogen, you can negate or reduce the damaging effects of exercise while not inhibiting the benefits of exercise, and in fact, maybe even potentiating the benefits of exercises. This is the idea that hydrogen in some ways can act as an exercise mimetic. Not in the true sense, but maybe it's a pseudo mimetic because it can activate some of the same metabolic pathways that exercise does.

And, in this case, it can maybe potentiate those benefits of exercise. Then again, to compare that to conventional antioxidants … taking high dose antioxidants can negate the benefits of exercise training.

Normally, with exercise you have improved insulin sensitivity, your glucose levels go down, you have better antioxidant status. Taking high levels of synthetic antioxidants can completely negate those benefits. So, again, hydrogen is superior because it doesn't do that."

How Molecular Hydrogen Rejuvenates Your Mitochondria

Interestingly, molecular hydrogen also induces **heat shock protein responses**, thereby mimicking some of the benefits of sauna therapy. One of the most important benefits of heat shock proteins is that they help refold misfolded proteins that no longer work properly and facilitates their removal if they can't be properly refolded.

Some of LeBaron's colleagues in Japan investigated this, showing molecular hydrogen is able to induce mtUPR, the mitochondrial unfolded protein response, which is thought to promote rejuvenation of the mitochondria. Molecular hydrogen has also been shown

to upregulate collagen biosynthesis, which is important both for youthfulness and post-injury healing.

More Information

So, to recap, the reason molecular hydrogen can have such diverse benefits in so many different disease models is because, essentially, all of them have excessive oxidative stress, redox dysregulation and inflammation as their root cause.

By regulating the oxidative pathways, molecular hydrogen can address these root causes. It's also selective and doesn't create reductive stress by avoiding making excessive antioxidants if your body doesn't need them.

For these reasons, it's my absolute favorite antioxidant and, I believe, the best option for most. One potential contraindication would be if you have small intestinal bowel overgrowth (SIBO), as, theoretically, those bacteria may feed on the hydrogen. This has not been confirmed, but it's a theoretical possibility. So, if you have SIBO, carefully evaluate how you feel after taking it.

If you want to take a deep dive into the science and application of molecular hydrogen, check out LeBaron's **courses, available at molecularhydrogeninstitute.org**. The institute offers four levels of certification, plus an apprentice course, but you don't have to be a health professional to take them.

> *"These courses are specifically designed to eradicate a lot of the misinformation, get the correct information out and allow you to think about how to use molecular hydrogen the best, how to optimize it and so on. So I think people are going to really like them,"* he says.

Sources and References

- [1] American Journal of Physiology 1996 Nov;271(5 Pt 1):C1424-37
- [2] Nature Medicine. May 7, 2007