Hydrogen Therapy: A emerging therapy with multiple biological functions and a long list of health benefits.

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Key Points

- Oxidative stress caused by free radicals, particularly Reactive Oxygen Species (ROS) damage and excessive chronic inflammation, are closely related to the pathogenesis of lifestyle related diseases.
- Hydrogen therapy has been shown to reduce oxidative stress and inflammation in humans and animals.
- By modulating cell signalling pathways and redox actions in the mitochondria, hydrogen therapy can act as a therapeutic agent in cardiovascular disease, metabolic disease, neurodegenerative disease and cancer.
- Hydrogen therapy, alongside a personalised movement and nutrition strategy, could modulate metabolic flexibility thereby aiding bodyfat and weight loss.
- Hydrogen therapy can cause acute and chronic changes in Heart Rate Variability which could improve sports performance and recovery via autonomic nervous system interaction.

INTRODUCTION

Hydrogen is a gas signalling molecule (GSM) which possesses multiple bioactivities including anti-inflammation and anti-reactive oxygen species (ROS) and could serve as a therapeutic agent in cancer, heart disease, metabolic disease, including diabetes and neuro-degenerative disease including Parkinson's, Alzheimer's and other dementias.

In humans, hydrogen (H_2), is produced from carbohydrates through the anaerobic metabolism of certain intestinal bacteria that contain the enzyme hydrogenase. These are carbohydrates that have not been absorbed by the intestine allowing the bacteria to feed on them. The resultant H_2 gas is then partially diffused into the bloodstream and released from the lungs by exhalation.

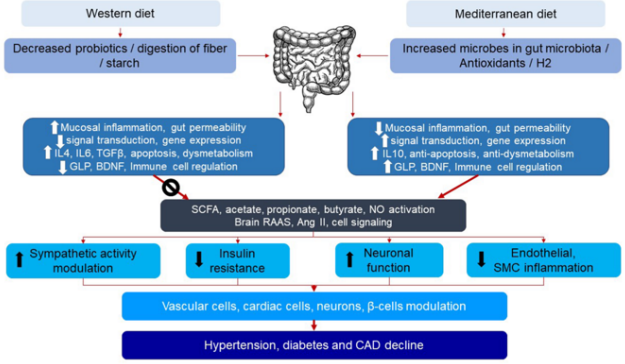


Figure 1
Mechanism of production and inhibition of molecular hydrogen due to diets via microbiota in the gut, and its effects on anti-inflammatory molecules and cardio-metabolic diseases.

H**2**, hydrogen; IL4, IL6, and IL10, interleukin 4, 6, and 10; TGF**β**, transforming growth factor beta; GLP, glucagon-like peptide; BDNF, brain-derived neurotrophic factor; SCFA, short-chain fatty acids; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system; Ang II, angiotensin II; CAD, coronary artery disease; SMC, smooth muscle cell.

RESEARCH OVERVIEW

Since 2007 over 2000 scientific publications have expounded the therapeutic use of Hydrogen Therapy in fighting disease in humans and animals yet, despite the compelling evidence, Hydrogen Therapy is yet to gain acceptance in in clinical settings.

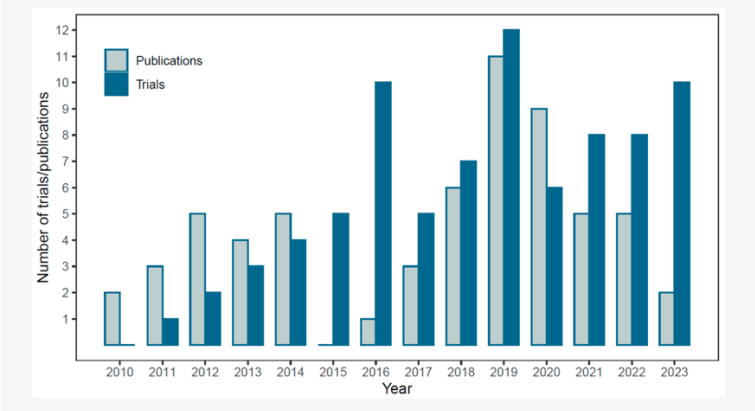


Figure 2
The number of clinical trials and scientific publications about hydrogen therapy in humans, sorted after publication year from 2010 to 2023 (per August 2023).

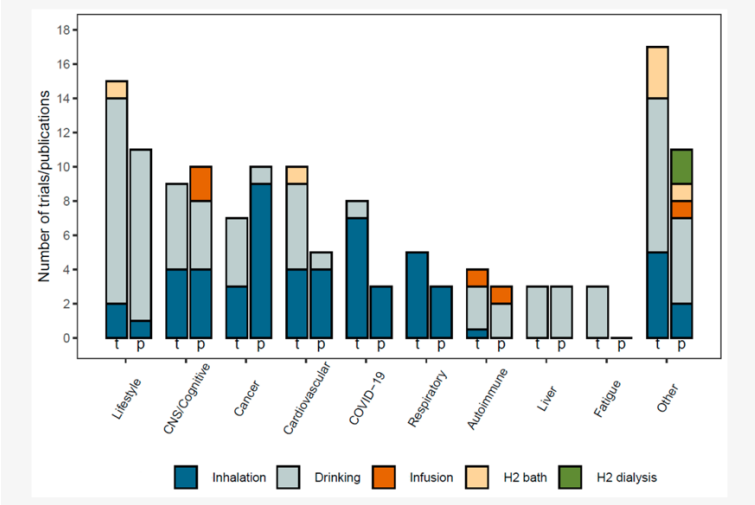
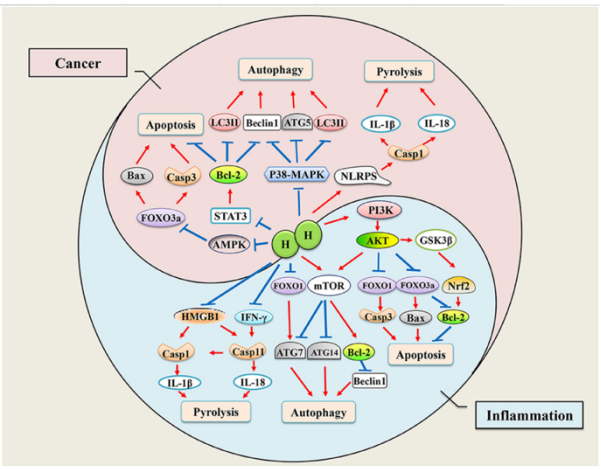


Figure 3
Registered clinical trials (t) and scientific publications (p) about hydrogen therapy, sorted by disease indication and administration method.

BIOLOGICAL MECHANISM

Figure 4

A schematic of the mechanism behind hydrogen regulating cell death. Hydrogen has bidirectional regulatory effects on apoptosis, autophagy, and pyrolysis.
When inflammation occurs, cells initiate apoptosis, autophagy, and pyroptosis to adapt to environmental changes, while hydrogen therapy ameliorates inflammation-induced excessive cell programmed death by regulating transcription of genes.
When a tumour occurs, hydrogen plays an antitumour role by promoting cell apoptosis, autophagy, and pyrolysis.



Peroxynitrite, ONOO- is now known to be implicated in an increasing number of diseases, including neurodegenerative disorders, atherogenesis and related cardiovascular diseases, diabetes, and immune and inflammatory disorders. H_2 is a specific scavenger of ONOO-.

Hydroxl Radical OH· Is the most biologically active free radical and its overabundance is linked to many diseases including cardiovascular disease, neurodegenerative disease and metabolic disease. H2 is also a specific scavenger of OH·.

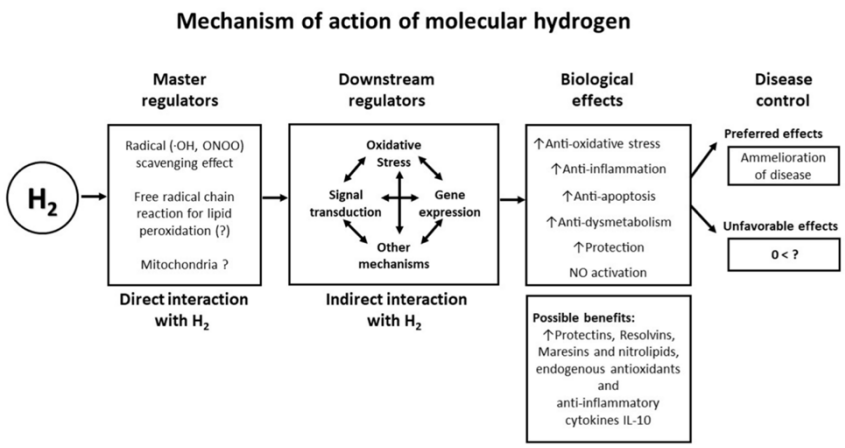


Figure 5 Mechanism of action of molecular hydrogen in the pathogenesis and control of cardiovascular and metabolic diseases (Modified from reference [11], Ichihara *et al.*, Med Gas Res 2015). ·OH, hydroxyl radical; ONOO**−**, peroxinitrite; H**2**, hydrogen; NO, nitric oxide; IL-10, interleukin 10.

HYDROGEN THERAPY & INFLAMMATION

Hydrogen therapy, also known as molecular hydrogen therapy, has gained attention in recent years for its potential anti-inflammatory and antioxidant properties. Here is a detailed overview of how hydrogen therapy might impact inflammation:

Mechanisms of Action

1. **Antioxidant Properties**: Molecular hydrogen (H2) can neutralize reactive oxygen species (ROS) and reduce oxidative stress, which is a major factor in inflammation. Unlike other antioxidants, hydrogen selectively reduces only the most harmful ROS, such as hydroxyl radicals, without disturbing other ROS that have physiological roles.
2. **Anti-inflammatory Effects**: Hydrogen therapy can downregulate pro-inflammatory cytokines and upregulate anti-inflammatory cytokines. This modulation helps reduce chronic inflammation and prevent the progression of inflammatory diseases.
3. **Cell Signaling Modulation**: Molecular hydrogen influences various signaling pathways involved in inflammation. It can inhibit pathways such as NF-κB and MAPK, which play crucial roles in the inflammatory response.

Applications in Inflammatory Conditions

1. **Rheumatoid Arthritis**: Studies have shown that hydrogen therapy can reduce symptoms and markers of inflammation in rheumatoid arthritis patients.
2. **Gastrointestinal Disorders**: Conditions such as inflammatory bowel disease (IBD) have been shown to improve with hydrogen-rich water, which can alleviate inflammation and oxidative stress in the gut.
3. **Neuroinflammation**: Hydrogen therapy has been explored for neurodegenerative diseases like Alzheimer's and Parkinson's, where chronic inflammation is a contributing factor.
4. **Respiratory Diseases**: In conditions such as chronic obstructive pulmonary disease (COPD) and asthma, hydrogen therapy has shown potential in reducing airway inflammation and oxidative stress.

Methods of Administration

1. **Hydrogen-Rich Water**: Drinking hydrogen-rich water is the most common method. The water is infused with molecular hydrogen, which is then ingested and absorbed into the body.
2. **Inhalation**: Inhaling hydrogen gas is another method, where hydrogen is mixed with oxygen and breathed in through a mask or nasal cannula.
3. **Topical Application**: Hydrogen-rich solutions can be applied directly to the skin for localized anti-inflammatory effects.
4. **Intravenous Administration**: This method involves injecting hydrogen-rich saline directly into the bloodstream for rapid systemic effects.

Clinical Evidence and Research

Research on hydrogen therapy is still emerging, but there are promising results from both animal studies and clinical trials:

- **Animal Studies**: Numerous studies have demonstrated the anti-inflammatory and antioxidant effects of hydrogen in various animal models of disease.
- **Clinical Trials**: Early-phase clinical trials have shown beneficial effects of hydrogen therapy in conditions like rheumatoid arthritis, metabolic syndrome, and chronic inflammation.

Safety and Side Effects

Hydrogen therapy is generally considered safe with minimal side effects. Hydrogen gas is non-toxic, and its concentrations used in therapy are far below explosive limits. Common side effects are rare and typically mild, such as minor gastrointestinal discomfort when consuming hydrogen-rich water.

Conclusion

Hydrogen therapy holds potential as a novel anti-inflammatory treatment due to its ability to selectively target oxidative stress and modulate inflammatory pathways. While more extensive clinical trials are needed to fully establish its efficacy and safety, current research indicates that hydrogen therapy could be a valuable addition to the management of inflammatory diseases.

HYDROGEN THERAPY & OXIDATIVE STRESS

Hydrogen therapy, particularly in the form of molecular hydrogen (H2), has shown promise in addressing oxidative stress. Oxidative stress results from an imbalance between reactive oxygen species (ROS) and the body's ability to detoxify these reactive intermediates or repair the resulting damage. Here's a detailed exploration of how hydrogen therapy interacts with oxidative stress:

Mechanisms of Action

1. **Selective Antioxidant Activity**:
   - **Neutralization of Harmful ROS**: Molecular hydrogen selectively reduces highly reactive and damaging ROS, such as hydroxyl radicals (·OH) and peroxynitrite (ONOO−), without affecting other ROS that play essential roles in cellular signalling.
   - **Maintaining Redox Balance**: By targeting specific ROS, hydrogen helps maintain the redox balance within cells, preventing oxidative damage while allowing beneficial ROS signaling to continue.
2. **Regulation of Antioxidant Enzymes**:
   - **Upregulation of Antioxidant Defenses**: Hydrogen therapy can stimulate the expression and activity of endogenous antioxidant enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase. This enhances the body's natural defense mechanisms against oxidative stress.
3. **Modulation of Cell Signaling Pathways**:
   - **Impact on Nrf2 Pathway**: Hydrogen can activate the Nrf2 (nuclear factor erythroid 2–related factor 2) pathway, which is a key regulator of cellular antioxidant responses. Activation of Nrf2 leads to the expression of various cytoprotective genes that combat oxidative stress.
   - **Inhibition of Pro-Oxidative Signaling**: Hydrogen therapy can inhibit pro-oxidative signaling pathways, such as NF-κB, which are often activated in response to oxidative stress and contribute to inflammation and cellular damage.

Applications in Oxidative Stress-Related Conditions

1. **Neurological Disorders**:
   - **Alzheimer's and Parkinson's Diseases**: Oxidative stress is a major factor in neurodegenerative diseases. Hydrogen therapy has shown potential in reducing oxidative damage and improving symptoms in these conditions.
   - **Stroke and Brain Injury**: Hydrogen gas has been investigated for its neuroprotective effects in stroke and traumatic brain injury, where oxidative stress plays a critical role in secondary injury.

2. **Cardiovascular Diseases**:
   - **Atherosclerosis**: By reducing oxidative stress, hydrogen therapy can help prevent the oxidation of low-density lipoprotein (LDL), a key step in the development of atherosclerosis.
   - **Myocardial Ischemia-Reperfusion Injury**: Hydrogen therapy has demonstrated protective effects against oxidative damage caused by

reperfusion following ischemia, improving cardiac function and reducing infarct size.

3. **Metabolic Disorders**:
    - **Diabetes**: Oxidative stress is implicated in the complications of diabetes. Hydrogen-rich water has shown promise in reducing oxidative stress markers and improving metabolic parameters in diabetic patients.
    - **Obesity**: Hydrogen therapy may help mitigate oxidative stress associated with obesity, potentially improving metabolic health and reducing inflammation.
4. **Chronic Inflammatory Conditions**:
    - **Rheumatoid Arthritis**: Inflammatory diseases like rheumatoid arthritis involve significant oxidative stress. Hydrogen therapy can reduce oxidative markers and alleviate symptoms.

Methods of Administration

1. **Hydrogen-Rich Water**: Drinking water infused with molecular hydrogen is the most common and accessible method. It allows for easy administration and systemic distribution of hydrogen.
2. **Inhalation**: Breathing in hydrogen gas, often mixed with oxygen, provides a rapid and direct way to increase hydrogen levels in the body.
3. **Topical Application**: Hydrogen-infused solutions can be applied to the skin to address localized oxidative stress and inflammation.
4. **Intravenous Administration**: Hydrogen-rich saline can be administered intravenously for immediate systemic effects, particularly in acute medical settings.

Clinical Evidence and Research

- **Animal Studies**: Numerous animal studies have demonstrated the efficacy of hydrogen therapy in reducing oxidative stress and improving outcomes in various disease models.
- **Human Studies**: Emerging clinical trials indicate that hydrogen therapy can reduce oxidative stress markers and improve clinical parameters in diseases like metabolic syndrome, diabetes, and neurodegenerative disorders.

Safety and Side Effects

Hydrogen therapy is considered safe, with no significant adverse effects reported at therapeutic doses. Hydrogen gas is non-toxic, and its use in clinical settings is well-tolerated. Mild side effects, such as gastrointestinal discomfort, are rare and typically associated with hydrogen-rich water ingestion.

Conclusion

Hydrogen therapy represents a promising approach to managing oxidative stress, leveraging its selective antioxidant properties and ability to modulate cellular defence mechanisms. As research progresses, hydrogen therapy could become a valuable tool in treating a wide range of conditions where oxidative stress plays a pivotal role.

HYDROGEN THERAPY & DISEASE

Cancer

Hydrogen therapy, particularly molecular hydrogen (H2) therapy, has been investigated for its potential therapeutic benefits, including its role in cancer treatment. The primary focus is on its antioxidant properties and its ability to reduce oxidative stress, which is implicated in cancer progression. Here are some insights based on current research:

1. Antioxidant Properties

Molecular hydrogen has been shown to selectively reduce harmful reactive oxygen species (ROS) and protect cells from oxidative damage. By mitigating oxidative stress, hydrogen therapy may help protect normal cells and tissues during cancer treatments like chemotherapy and radiation, which generate high levels of ROS.

2. Anti-Inflammatory Effects

Hydrogen therapy may also exert anti-inflammatory effects. Chronic inflammation is known to contribute to the development and progression of cancer. By reducing inflammation, hydrogen therapy might inhibit cancer cell proliferation and metastasis.

3. Animal and Preclinical Studies

Preclinical studies have demonstrated that hydrogen-rich water can inhibit the growth of certain types of tumours in animal models. For instance, some studies have shown reduced tumour growth in mice treated with hydrogen-rich water, suggesting a potential therapeutic benefit.

4. Protective Effects Against Chemotherapy-Induced Toxicity

There is evidence that hydrogen therapy can alleviate the side effects of chemotherapy. For example, hydrogen-rich water has been reported to reduce cisplatin-induced nephrotoxicity (kidney damage) and other side effects in animal studies and small clinical trials.

5. Clinical Evidence

Human studies on hydrogen therapy for cancer are still limited and primarily in the early stages. Some small-scale clinical trials and case reports suggest benefits.

Overall, while hydrogen therapy shows promise as an adjunctive treatment for cancer, particularly in reducing treatment-related side effects and potentially inhibiting tumour growth, it is not yet a mainstream or standalone treatment. Patients interested in hydrogen therapy should consult with their healthcare providers and consider it within the context of conventional cancer treatments and clinical trials.

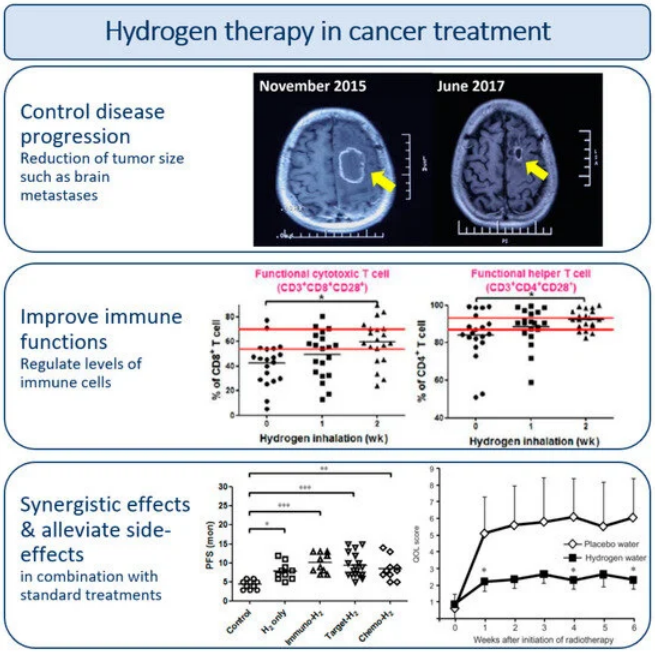


Figure 6
Schematic overview of the effects of hydrogen therapy in cancer treatment. The top images show MR imaging of brain metastasis (arrow) before (**left**) and after (**right**) H_2 treatment.

The middle figures show alterations in cytotoxic and helper T cell levels in cancer patients after H_2 treatment.

The parallel red lines show the normal range of cell levels, and the black short lines show the measured average values at each time point.

The bottom left figure shows number of months (mon) with progression-free survival (PFS) of lung cancer patients receiving no treatment (control), H_2 therapy (H_2 only), or combined treatments with H_2 and immunotherapy (immuno), targeted therapy (target) or chemotherapy (chemo). The black short lines show the average PFS values for each treatment.

The bottom right figure shows the quality of life (QOL) scores of patients treated with radiotherapy for liver tumours with or without H_2 water. A higher score reflects more symptoms and lower QOL.

Heart Disease

Hydrogen therapy has emerged as a potential therapeutic intervention for various diseases, including cardiovascular disease (CVD). The use of molecular hydrogen (H_2) as a medical gas or in hydrogen-rich water has been studied for its potential antioxidative, anti-inflammatory, and anti-apoptotic effects.

Mechanisms of Action

1. **Antioxidative Properties**:
   - **Reduction of Oxidative Stress**: Molecular hydrogen can selectively reduce highly reactive oxygen species (ROS) such as hydroxyl radicals, which are implicated in oxidative stress and damage to cardiovascular tissues.
   - **Protection of Mitochondria**: By reducing oxidative stress, hydrogen helps protect mitochondrial function, which is crucial for maintaining energy production in heart cells.
2. **Anti-inflammatory Effects**:
   - **Modulation of Inflammatory Pathways**: Hydrogen has been shown to modulate signalling pathways that control inflammation, potentially reducing chronic inflammation associated with cardiovascular diseases.

- **Reduction of Pro-inflammatory Cytokines**: Studies indicate that hydrogen therapy can decrease the levels of pro-inflammatory cytokines, thereby mitigating inflammatory responses in cardiovascular tissues.

3. **Anti-apoptotic Effects**:
   - **Cell Survival**: Hydrogen therapy has been reported to promote cell survival and reduce apoptosis (programmed cell death) in cardiac cells, which is beneficial in conditions like myocardial infarction (heart attack).

Clinical and Experimental Evidence

1. **Animal Studies**:
   - **Myocardial Infarction**: Animal models of myocardial infarction treated with hydrogen have shown reduced infarct sizes and improved cardiac function.
   - **Heart Failure**: Studies in animals have demonstrated that hydrogen can improve cardiac function and reduce pathological changes associated with heart failure.
2. **Human Studies**:
   - **Pilot Studies**: Some early-phase clinical trials in humans have shown promising results, such as improved endothelial function and reduced markers of oxidative stress and inflammation in patients with cardiovascular disease.
   - **Safety and Tolerability**: Hydrogen therapy has generally been well-tolerated in human studies, with few reported side effects.

Methods of Administration

1. **Inhalation**: Inhaling hydrogen gas (typically mixed with air or oxygen) through a mask or ventilator.
2. **Hydrogen-rich Water**: Drinking water that has been infused with molecular hydrogen.
3. **Intravenous Hydrogen-rich Saline**: Administration of saline solution saturated with hydrogen.

Potential Benefits

1. **Cardioprotection**: Hydrogen therapy may offer protection against ischemia-reperfusion injury (damage caused when blood supply returns to the tissue after a period of ischemia or lack of oxygen).

2. **Improved Vascular Function**: By reducing oxidative stress and inflammation, hydrogen therapy can improve endothelial function, which is critical for maintaining healthy blood vessels.
3. **Reduced Hypertension**: Some studies suggest that hydrogen therapy may help lower blood pressure by improving vascular function and reducing oxidative stress.

In summary, hydrogen therapy holds promise as a novel treatment for cardiovascular disease, offering potential benefits through its antioxidative, anti-inflammatory, and anti-apoptotic properties. However, further research is needed to validate these findings and to establish clinical guidelines for its use.

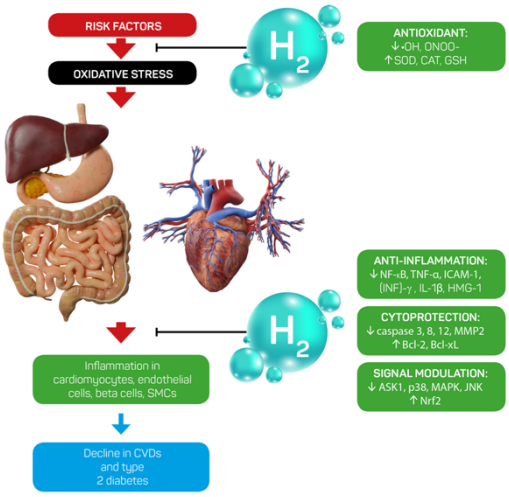


Figure 7
Mechanisms of the effects of hydrogen therapy on cardio-metabolic disease. SMCs, smooth muscle cells; CVDs, cardiovascular diseases; NF-**κ**B, nuclear factor kappa B; TNF-**α**, tumor necrosis factor alpha; ICAM-1, inter cellular adhesion molecule-1; (INF)-**γ**, interferon gamma; IL-1**β**, interleukin 1 beta; HMG-1, high mobility group box 1 protein; MMP2, matrix metalloproteinase 2; Bcl-2, B-cell lymphoma 2; Bcl-xL, B-cell lymphoma-extra-large; ASK1, apoptosis signal-regulating kinase 1; MAPK, mitogen-activated protein kinase; JNK, c-Jun N-terminal kinases; Nrf2, nuclear factor erythroid 2-related factor 2; ·OH, hydroxyl radical; ONOO**−**, peroxinitrite; SOD, superoxide dismutase; CAT, catalase; GSH, glutathione; H**2**, hydrogen.

Metabolic Disease

Hydrogen therapy is being investigated for its potential benefits in treating metabolic diseases, which include conditions like diabetes, obesity, and metabolic syndrome. The therapeutic properties of molecular hydrogen (H_2) are largely attributed to its antioxidative, anti-inflammatory, and cellular protective effects. Here's an overview of how hydrogen therapy may impact metabolic diseases:

Mechanisms of Action

1. **Antioxidative Properties**:
   - **Reduction of Oxidative Stress**: Molecular hydrogen selectively reduces harmful reactive oxygen species (ROS), such as hydroxyl radicals, which contribute to oxidative stress in metabolic diseases.

- **Protection of Mitochondria**: By mitigating oxidative stress, hydrogen helps maintain mitochondrial function, which is crucial for energy metabolism and insulin sensitivity.

2. **Anti-inflammatory Effects**:
   - **Modulation of Inflammatory Pathways**: Hydrogen can influence signaling pathways that control inflammation, potentially reducing chronic inflammation associated with metabolic diseases.
   - **Reduction of Pro-inflammatory Cytokines**: Hydrogen therapy can decrease levels of pro-inflammatory cytokines, which are elevated in conditions like obesity and diabetes.
3. **Cellular Protection**:
   - **Prevention of Apoptosis**: Hydrogen may protect cells from apoptosis (programmed cell death) induced by oxidative stress and inflammation, supporting tissue health and function.
   - **Insulin Sensitivity**: By reducing oxidative stress and inflammation, hydrogen may improve insulin signaling pathways, enhancing insulin sensitivity.

Clinical and Experimental Evidence

1. **Animal Studies**:
   - **Diabetes**: Animal models of diabetes treated with hydrogen have shown improved blood glucose levels, increased insulin sensitivity, and protection of pancreatic beta cells.
   - **Obesity**: Studies in obese animals have demonstrated that hydrogen therapy can reduce body weight, lower lipid levels, and improve metabolic markers.
2. **Human Studies**:
   - **Type 2 Diabetes**: Preliminary clinical trials in patients with type 2 diabetes have shown that hydrogen-rich water can improve glucose metabolism, reduce oxidative stress markers, and enhance insulin sensitivity.
   - **Metabolic Syndrome**: Some studies suggest that hydrogen therapy can help ameliorate various components of metabolic syndrome, such as hypertension, dyslipidaemia and insulin resistance.

Potential Benefits

1. **Blood Glucose Control**: Hydrogen therapy may help regulate blood sugar levels, reducing hyperglycaemia in diabetic patients.
2. **Weight Management**: By improving metabolic function and reducing inflammation, hydrogen therapy could support weight loss and management.
3. **Lipid Profile Improvement**: Hydrogen may help lower cholesterol and triglyceride levels, contributing to better cardiovascular health.
4. **Insulin Sensitivity**: Enhanced insulin sensitivity can lead to better glucose uptake by cells, improving overall metabolic health.

Summary

Hydrogen therapy shows potential as a novel treatment for metabolic diseases, offering benefits through its antioxidative, anti-inflammatory, and cellular protective properties. Early research, both in animal models and preliminary human trials, indicates that hydrogen therapy can improve metabolic health markers, enhance insulin sensitivity, and reduce inflammation. However, more extensive and long-term studies are necessary to establish clinical guidelines and confirm its efficacy and safety for widespread use in metabolic disease management.

Neuro-degenerative Disease

Hydrogen therapy is being explored for its potential therapeutic effects on neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease. The proposed benefits are largely due to hydrogen's antioxidative, anti-inflammatory, and neuroprotective properties. Here's a detailed overview of the potential relationship between hydrogen therapy and neurodegenerative diseases:

Mechanisms of Action

1. **Antioxidative Properties**:
   - **Reduction of Oxidative Stress**: Molecular hydrogen selectively scavenges highly reactive oxygen species (ROS) like hydroxyl radicals, which contribute to neuronal damage in neurodegenerative diseases.

- **Mitochondrial Protection**: By reducing oxidative stress, hydrogen helps protect mitochondrial function, crucial for energy production and neuronal health.

2. **Anti-inflammatory Effects**:
   - **Modulation of Inflammatory Pathways**: Hydrogen influences inflammatory signaling pathways, potentially reducing chronic inflammation that exacerbates neurodegenerative conditions.
   - **Reduction of Pro-inflammatory Cytokines**: Hydrogen therapy can decrease levels of pro-inflammatory cytokines, thereby mitigating inflammatory responses in the brain.
3. **Neuroprotection**:
   - **Prevention of Apoptosis**: Hydrogen may prevent apoptosis (programmed cell death) in neurons caused by oxidative stress and inflammation.
   - **Improvement in Neurogenesis**: Hydrogen might enhance neurogenesis, the process of generating new neurons, which is crucial for maintaining cognitive functions.

Clinical and Experimental Evidence

1. **Animal Studies**:
   - **Alzheimer's Disease**: Animal models treated with hydrogen have shown reduced amyloid-beta plaques, decreased oxidative stress, and improved cognitive function.
   - **Parkinson's Disease**: Hydrogen therapy in animal models has demonstrated neuroprotective effects, such as reduced dopaminergic neuronal loss and improved motor function.
   - **ALS and Huntington's Disease**: Studies in animal models have indicated that hydrogen can mitigate neuronal damage and improve survival rates.
2. **Human Studies**:
   - **Pilot Studies**: Some early-phase clinical trials in humans with neurodegenerative diseases have shown promising results, such as improved cognitive function, reduced oxidative stress markers, and enhanced quality of life.
   - **Safety and Tolerability**: Hydrogen therapy has been generally well-tolerated in human studies, with few reported side effects.

Methods of Administration

1. **Inhalation**: Inhaling hydrogen gas (typically mixed with air or oxygen) through a mask or nasal cannula.
2. **Hydrogen-rich Water**: Drinking water infused with molecular hydrogen.
3. **Hydrogen-rich Saline**: Intravenous administration of saline solution saturated with hydrogen.

Potential Benefits

1. **Cognitive Function**: Hydrogen therapy may help preserve cognitive functions and slow down cognitive decline in diseases like Alzheimer's.
2. **Motor Function**: In diseases such as Parkinson's, hydrogen therapy could improve motor function and reduce symptoms.
3. **Neuronal Protection**: By reducing oxidative stress and inflammation, hydrogen therapy can protect neurons and support overall brain health.
4. **Quality of Life**: Hydrogen therapy might improve the quality of life for patients with neurodegenerative diseases by alleviating some symptoms and slowing disease progression.

Summary

Hydrogen therapy holds promise as a novel treatment for neurodegenerative diseases, offering potential benefits through its antioxidative, anti-inflammatory, and neuroprotective properties. Early research, including animal studies and preliminary human trials, suggests that hydrogen therapy can improve cognitive and motor functions, reduce neuronal damage, and enhance quality of life. However, further extensive and long-term studies are necessary to confirm these findings and to establish clinical guidelines for its use in managing neurodegenerative diseases.

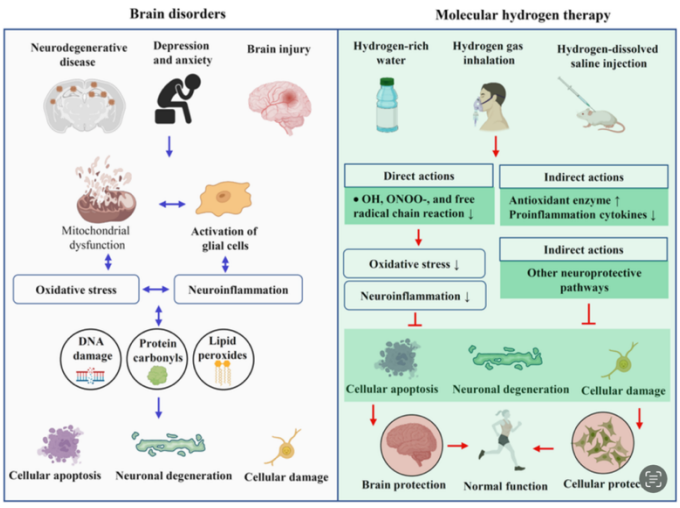


Figure 8
Primary mechanisms of molecular hydrogen therapies in brain disorders. Nearly all neuro-degenerative diseases, brain injuries, and mood disorders are characterized by mitochondrial function and neuroinflammation.
The dysfunction of mitochondria induces excessive production of ROS and the excessively released inflammatory cytokines, which further damage mitochondria and active glial cells. All these changes induce oxidative damage to DNA, protein, and lipids, which finally induce cellular damage, neuronal degeneration, and neuronal loss. However, hydrogen works as an electron donor to selectively scavenge the excessive hydroxyl radical to reduce oxidative stress directly. Additionally, hydrogen enhances the activity of antioxidant enzymes, reduces the release of proinflammatory factors, and activates other neuroprotective pathways.

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Richard is an expert in using nutrition and movement interventions to improve the health, fitness and function of adults over 50 and his research in this area has been published in peer reviewed scientific journals. His current area of research is in Heart Rate Variability and Metabolic Flexibility and the relationship between these two measurements with inflammation and oxidative stress.

"By reducing inflammation and oxidative stress I have seen clients with cardiovascular disease, diabetes, muscle and joint pain, dementia and cancer improve their condition and get another chance at living as healthy & fulfilling life. Following an expertly designed and strategically managed personalised movement and nutrition plan is essential in order to live your healthiest lifestyle and beat degenerative disease."

Richard sees private clients by appointment in London and the home counties.

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Glossary

- **Antioxidants**

Molecules that neutralise free radicals breaking harmful chain reactions within cells. Antioxidants can be found in plant-based foods. Organic, wholefood sources of antioxidants are far more effective than supplement sources.

- **Apoptosis**

Apoptosis is programmed cell death. Billions of cells in the human body die every hour to accommodate the growth of new cells and to facilitate adaptation to one's environment. If you are sedentary then you do not need the requisite heart, lung, blood and muscles cells needed for movement – this is why sedentary behaviour reduces one's capacity, you really do 'use it or lose it'. Certain lifestyle choices, diseases and environmental exposure to pollutants, such as cigarette smoke, car and plane emissions as well as stress, lack of sleep, etc. can lead to an increase is apoptosis at a rate that can cause accelerated aging of tissue such including bone, muscle nerves and skin.

- **Cardiovascular Disease**

An umbrella term including any disease of the heart or blood vessels and includes coronary artery disease and cerebrovascular disease, peripheral artery disease and congenital heart disease.

- **Cytokines**

Signalling proteins used as chemical messengers by the immune system. Whilst cytokines are a necessary part of immune system function, some infections can cause an excessive cytokine response which can result in elevated inflammation. Chronically high cytokine levels created by inappropriate lifestyle choices can lead to autoimmune diseases as well as other diseases associated with chronic levels of inflammation.

- **Free Radicals**

Molecules that are created through completely natural endogenous physiological processes but, increasingly in our society, they are also produced through exposure to exogenous sources such as air pollutants, cigarette smoking and industrial chemicals. They include reactive oxygen species and reactive nitrogen species. The chemical structure of these molecules (they have an unpaired electron) is such that, in the absence of sufficient antioxidants, they can cause biological damage an increase the likelihood and severity of cancer, heart disease, metabolic disease and neurodegenerative disease.

- **Heart Rate Variability**

An indicator of the state of your autonomic nervous system as measured by the distance between heart beats. Minor changes, measured in milliseconds, between heart beats can indicate whether the Sympathetic Nervous System (the fight or flight response) or the Parasympathetic Nervous System (the rest, repair and regenerate response) is dominant. Chronic low HRV can indicate the onset of disease in advance of symptoms and blood tests.

- **Inflammation**

A natural part of your bodies immune system, inflammation can help repair damaged tissue. However, in the presence of chronic inflammation the likelihood of certain diseases developing, including cardiovascular disease, metabolic disease and arthritis amongst many others, is much greater.

Glossary cont.

- **Metabolic Disease**

Becoming more and more common, people with a history of smoking, sedentary behaviour, obesity, particularly a high level of abdominal fat and chronic issues with sleep are more likely to have problems regulating blood sugar levels, responding to insulin and regulating blood lipids and cholesterol. Type II diabetes, cardiovascular disease, neurodegenerative disease can cancer have all been associated with metabolic disorder or metabolic syndrome.

- **Metabolic Flexibility**

The ability to respond and adapt to changes in metabolic demand. If you are sitting, working at your desk and you have good metabolic flexibility you would be using fat as your primary fuel source. If you had to suddenly run for a bus you would be able to quickly move to using carbohydrate as an energy source as it provides energy at a much faster rate. Certain lifestyle choices, inappropriate nutrition, poorly designed exercise programs, stress, lack of sleep can negatively affect ones metabolic flexibility leading to weight gain, difficulty losing bodyfat, poor attention spans, brain fog, tiredness, increased appetite and problems sleeping.

- **Mitochondria**

Often described as the 'powerhouses' of our cells these tiny structures are essential for human existence. Mitochondria contain the cellular apparatus to provide us with the energy we need to move and perform our normal daily functions. However, this is only one role of the mitochondria. Other roles include regulating cellular metabolism, steroid synthesis, calcium regulation and apoptosis. Effective training programs can increase the size and number of mitochondria in our muscles making movement easier and improving metabolic flexibility and heart rate variability.
Mitochondrial dysfunction can lead to Parkinson's, Alzheimer's, Chronic Fatigue Syndrome, Diabetes and problems with the heart, liver, kidneys and gastrointestinal system.

- **Neurodegenerative Disease**

Characterised by a loss of neurons either centrally, in the brain, or peripherally, in the nerves. ND affects millions of people each year all over the world and is on the increase both in numbers and percentage population affected. Alzheimer's and Parkinson's are the most common neurodegenerative disorders. Whilst a small percentage may be linked to a genetic cause, the research is increasingly pointing to certain lifestyle factors as causative such as sedentary behaviour, inappropriate nutrition, poor sleep quality, exposure to environmental pollutants and alcohol consumption.

- **Oxidative Stress**

A phenomenon caused by an imbalance between production of free radicals within a cell and that cell's ability to clear them out. Oxidative stress is linked to cardiovascular disease, metabolic disease, neurodegenerative disease, kidney disease, respiratory disease and cancer.

- **Reactive Oxygen Species**

A group of free radicals including superoxide anion radical, hydroxl radical and hyperoxl radical. These some of the most damaging and destructive molecules that we know of.