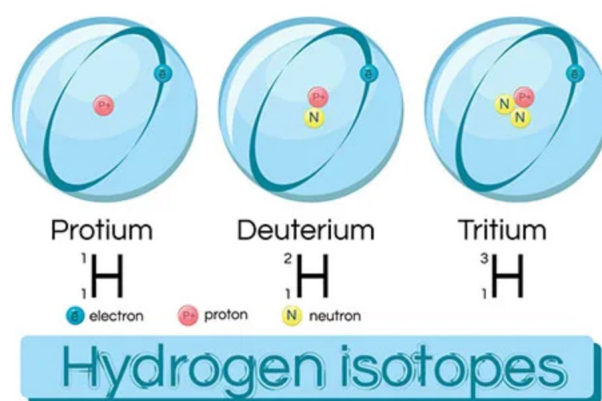


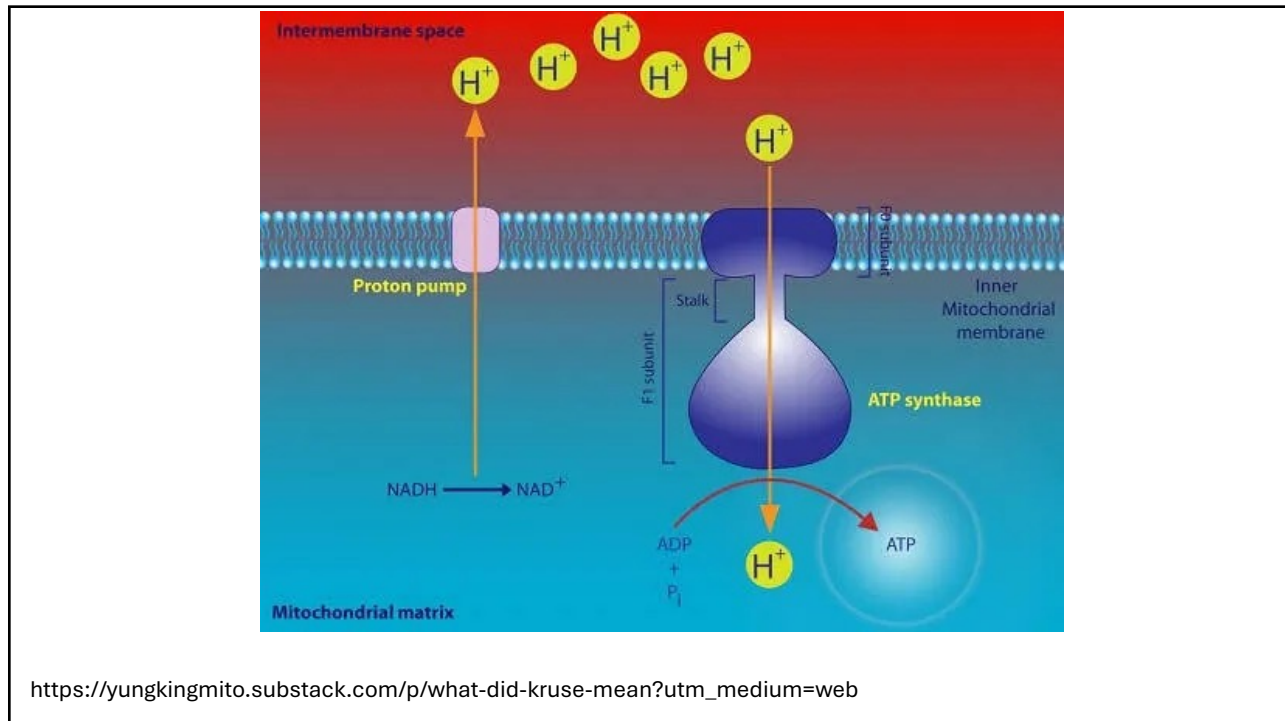
Deuterium Depleted Water and Health

1



Research suggests consuming Deuterium-Depleted Water (DDW) may improve metabolic health, enhance mitochondrial efficiency, and inhibit the proliferation of certain cancer cells. By lowering the body's natural deuterium levels, DDW is thought to reduce the kinetic isotope burden on cellular enzymes, promoting optimal energy production and cellular repair.

2



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The distribution of deuterium differs geographically and climatically in a few distinct ways:

- **The Latitude Effect:** As oceanic water vapor travels from the warm equator toward the poles, it cools and progressively rains out its heavy isotopes. As a result, polar precipitation contains significantly less deuterium than equatorial or coastal waters.
- **The Altitude Effect:** As air masses rise over mountain ranges, they expand, cool, and lose moisture. Because deuterium-rich water vapor condenses preferentially, the remaining precipitation at higher elevations becomes increasingly "depleted" of heavy isotopes.
- **Deuterium Depletion Values:** Deuterium levels are measured in parts per million (ppm) relative to ocean water. *Sea-level water typically contains about 150 ppm of deuterium, while mountainous regions or areas at high latitudes (like Antarctica) can see levels drop to as low as 130 ppm*

<https://www.sciencedirect.com/topics/physics-and-astronomy/meteoric-water>

4

frontiers

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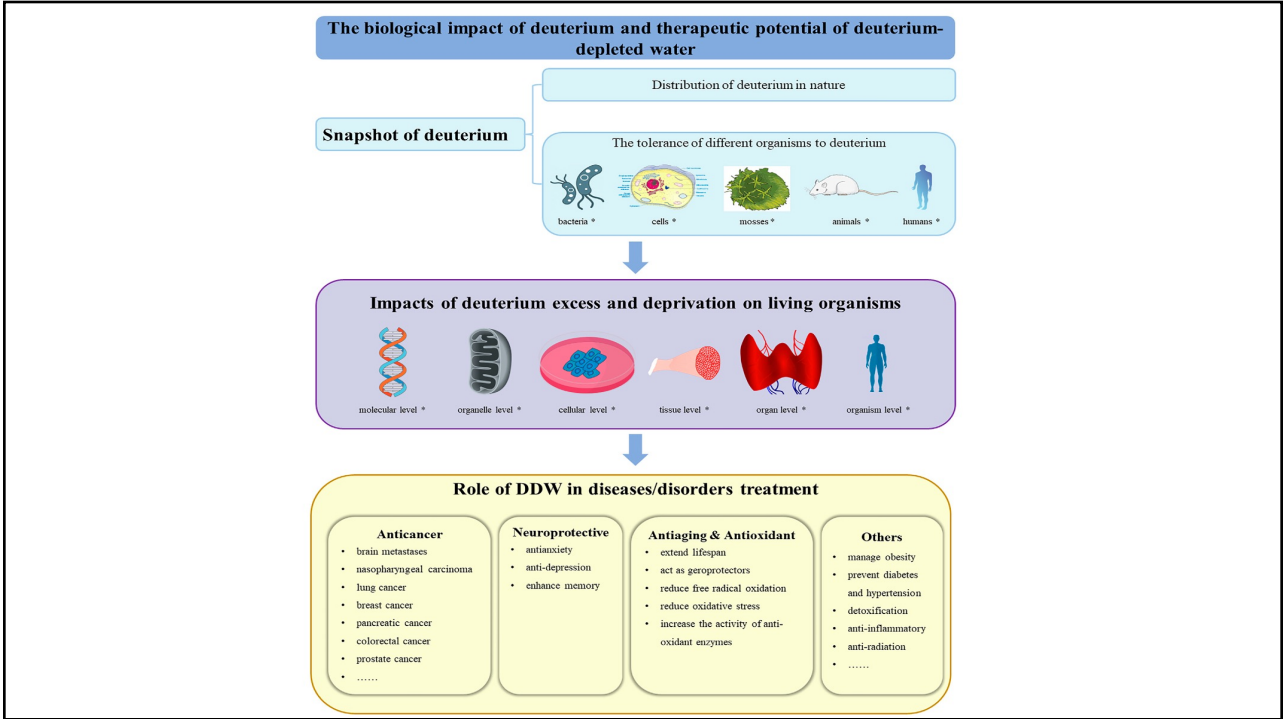
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The biological impact of deuterium and therapeutic potential of deuterium-depleted water

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Deuterium Depleted Water and Health

- **Cancer Therapy & Prevention:** Much of the existing literature highlights DDW's potential to inhibit the proliferation of tumor cells by inducing cell cycle arrest and apoptosis (programmed cell death). Clinical observations, such as a prominent Hungarian study of prostate cancer patients, have reported significantly extended median survival times when DDW was combined with conventional therapies.
- **Diabetes & Metabolic Syndrome:** Preclinical and early-stage clinical data suggest that DDW can stimulate glucose uptake (translocation of GLUT4) in the presence of insulin. Research indicates this can lead to decreased blood glucose concentrations and help harmonize metabolic syndrome markers.
- **Neurological & Mood Health:** Animal studies and epidemiological data indicate a link between high deuterium levels and depression, suggesting that deuterium-depleted environments may elicit anxiolytic (anti-anxiety) behaviors and support long-term memory functions.
- **Anti-Aging & Antioxidant Effects:** By facilitating more efficient mitochondrial function, reduced deuterium loads are being investigated for their role in mitigating age-associated cellular decay and increasing the activity of endogenous antioxidant enzymes (like catalase and superoxide dismutase)

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Deuterium Depleted Water and Health

Ultraviolet (UV) Light

Isotope Effects on Absorption: Both standard water and heavy water are largely transparent to visible light, but they begin absorbing heavily in the deep UV spectrum (below 200 nm). *The isotopic substitution affects the strength and length of the oxygen-deuterium bond, changing how the molecule absorbs and scatters shorter UV wavelengths.*

Biological Sensitivity: Exposing biological molecules (like proteins) to UV radiation produces different outcomes depending on whether they are suspended in standard water H₂O or heavy water D₂O. The substitution alters the *hydration shell and the stability of the protein structure, changing its sensitivity to UV-induced damage*

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Deuterium Depleted Water and Health

Infrared (IR) Light

Molecular Vibration: Deuterium is twice as heavy as standard hydrogen. When IR light hits deuterium in water, the extra neutron in the deuterium nucleus changes the mass of the atom, which significantly reduces the frequency of the molecule's vibrations.

Absorption Shifts: While standard H₂O absorbs specific bands of IR light, the heavier bonds in D₂O shift these absorption peaks to longer IR wavelengths.

Exclusion Zone (EZ) Water: In cellular biology, absorbing near-infrared (NIR) light causes water molecules near hydrophilic surfaces to align into a gel-like, deuterium-depleted state. IR absorption is used here to physically organize and separate deuterium-rich water from deuterium-depleted zones.

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RESEARCH ARTICLE

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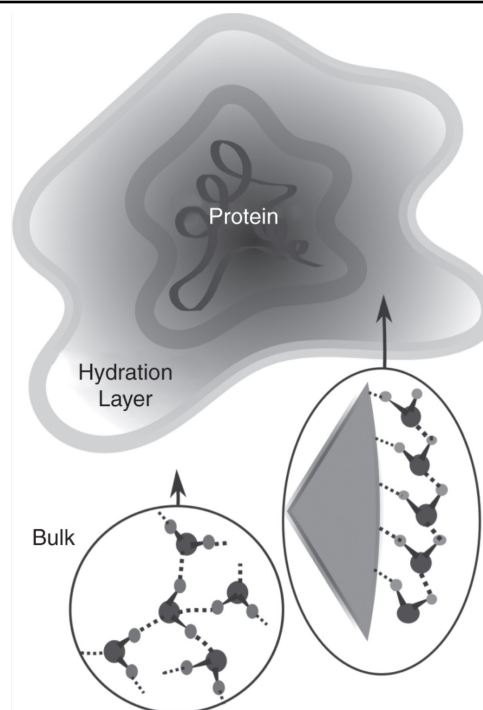
Spatial Layouts of Low-Entropy Hydration Shells Guide Protein Binding

Lin Yang,* Shuai Guo, Chenchen Liao, Chengyu Hou, Shenda Jiang, Jiacheng Li, Xiaoliang Ma, Liping Shi, Lin Ye, and Xiaodong He*

Protein-protein binding enables orderly biological self-organization and is therefore considered a miracle of nature. Protein-protein binding is driven by electrostatic forces, hydrogen bonding, van der Waals force, and hydrophobic interactions. Among these physical forces, only hydrophobic interactions can be considered long-range intermolecular attractions between proteins due to the electrostatic shielding of surrounding water molecules. Low-entropy hydration shells around proteins drive hydrophobic attraction among them that essentially coordinate protein-protein binding. Here, an innovative method is developed for identifying low-entropy regions of hydration shells of proteins by screening off pseudohydrophilic groups on protein surfaces and revealing that large low-entropy regions of the hydration shells typically cover the binding sites of individual proteins. According to an analysis of determined protein complex structures, shape matching between a large low-entropy hydration shell region of a protein and that of its partner at the binding sites is revealed as a universal law. Protein-protein binding is thus found to be mainly guided by hydrophobic collapse between the shape-matched low-entropy hydration shells that is verified by bioinformatics analyses of hundreds of structures of protein complexes, which cover four test systems. A simple algorithm is proposed to accurately predict protein binding sites.

Protein-protein binding is a spontaneous physical contact of high specificity, established between two specific protein molecules, and protein-protein binding is highly rare in extracellular fluid.^[1] At present, it is generally accepted that protein-protein binding does not violate the second law of thermodynamics because the binding state is most likely a state of maximum entropy of the extracellular or intracellular aqueous solution system. The physical mechanism responsible for protein-protein binding can be considered the most important mechanism of biological self-organization, functionalization, and diversity.

The July 1, 2005 issue of Science published a list of 125 important questions in science, one of the questions is "How do proteins find their partners?"^[2] Even though significant progress has been made toward the structural determination of protein complexes, many complexes that are crucial drug targets for cancer and diseases remain



Global Challenges. 2023, 7, 2300022

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Heavy Water Effects Protein Structure and Function	
Function	How the Hydration Shell Helps
Protein Folding	As an unfolded protein folds into its 3D shape, nonpolar side chains are buried inside. This strips away portions of the hydrophobic hydration shell, releasing water molecules and creating an energetic drive (hydrophobic effect) that forces the protein to fold.
Enzyme Catalysis	The mobility of water molecules in the shell acts as a "lubricant" that gives the protein the flexibility needed to change shape and catalyze chemical reactions.
Molecular Recognition	When a protein binds to a drug, DNA, or another protein, matching patches on their hydration shells must match up or displace water to allow the two molecules to lock together tightly.

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Metabolomics (2024) 20:117
<https://doi.org/10.1007/s11306-024-02173-4>



Nutritional deuterium depletion and health: a scoping review

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Abstract

Introduction Large variations in fatty and amino acid natural ²H/¹H ratios in reference with solvent water point to the active involvement of compartmental, inter- and intramolecular deuterium disequilibrium in adaptive biology. Yet, the human deutenome is an untapped area of energy metabolism and health in humans.

Objectives The purpose of this scoping review is to examine health effects through deuterium homeostasis using deuterium-depleted water and/or a deuterium-depleted diet. We also aim to reveal health effects of nutritional, metabolic and exercise ketosis, i.e. complete mitochondrial fatty acid oxidation with the production of deuterium depleted (depleted) metabolic water.

Methods A protocol process approach was used to retrieve current research in deuterium depletion according to the preferred reporting items protocol for systematic reviews and meta-analyses, extension for scoping reviews with checklist (PRISMA-ScR).

Results Fifteen research articles were used. All retrieved articles were heterogenous in nature and additional themes did not evolve. Deuterium depletion was found to have beneficial health effects in the following conditions: cancer prevention, cancer treatment, depression, diabetes, long-term memory, anti-aging, and sports performance. Deutenomics is actively pursued in drug research and there are biomarker roles attributed to large natural variations with adaptive significance in biology.

Conclusion Even with limited data, consistent deuterium depletion can be seen across all conditions reviewed. More randomized control trials are recommended to confirm cause and effect for translationally and clinically informed integrative nutrition-based medical interventions.

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Article

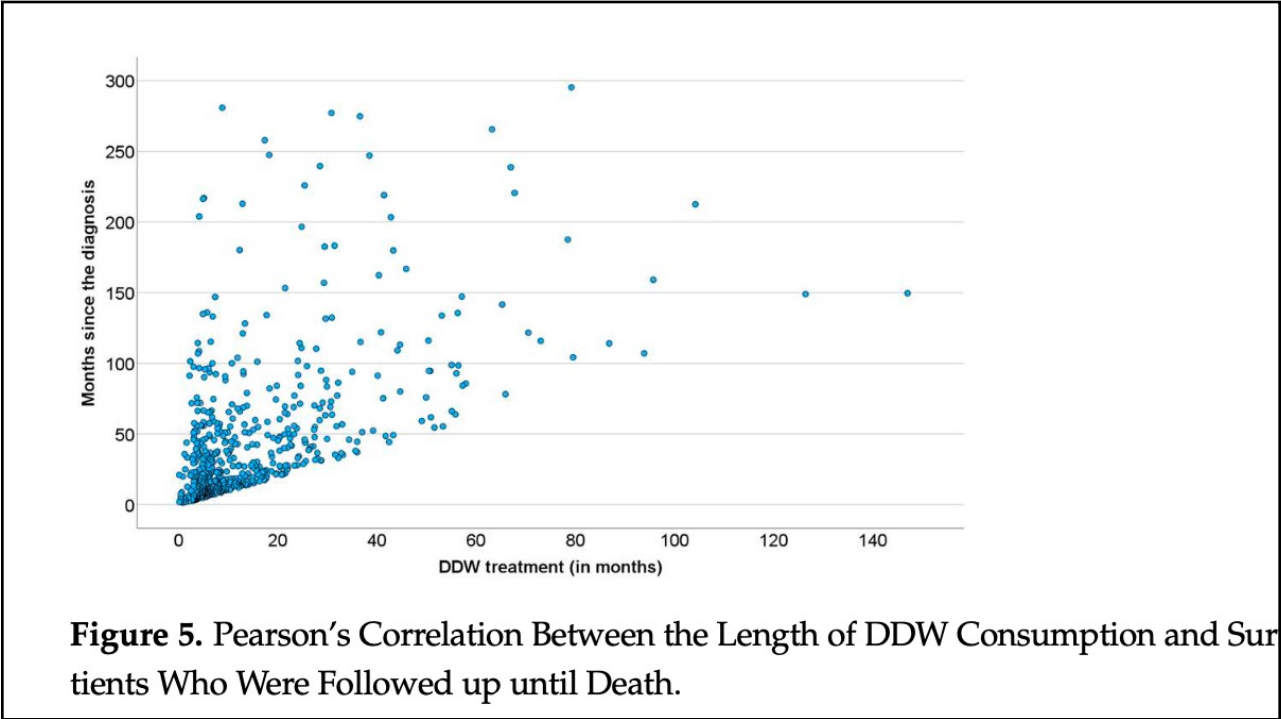
Real-World Data Confirm That the Integration of Deuterium Depletion into Conventional Cancer Therapy Multiplies the Survival Probability of Patients

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Abstract: **Background:** Over thirty years of basic research has demonstrated that the deuterium-to-hydrogen ratio plays a pivotal role in regulating metabolism and cell growth via a sub-molecular regulatory system that orchestrates the intricate complexity of life in eukaryotic organisms. Deuterium depletion, achieved through deuterium-depleted water (DDW), has shown anticancer effects in vitro, in vivo, and in Phase 2 prospective and retrospective clinical studies. **Methods:** In this population-based observational study, 2649 cancer patients undergoing conventional therapy and consuming DDW were included between October 1992 and October 2024. With various cancer types and stages and conventional therapies received, they are representing a broad spectrum of the Hungarian

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Systematic Review

Deuterium-Depleted Water in Cancer Therapy: A Systematic Review of Clinical and Experimental Trials

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Abstract: Chemotherapy exhibits numerous side effects in anti-tumour therapy. The clinical experiments indicated that deuterium-depleted water (DDW) monotherapy or in combination with chemotherapy was beneficial in inhibiting cancer development. To further understand the potential mechanism of DDW in cancer therapy, we performed a systematic review. The data from experiments published over the past 15 years were included. PubMed, Cochrane and Web of Science (January 2008 to November 2023) were systemically searched. Fifteen studies qualified for review, including fourteen in vivo and in vitro trials and one interventional trial. The results showed that DDW alone or in combination with chemotherapy effectively inhibited cancer progression in most experiments. The combination treatment enhances the therapeutic effect on cancer compared with chemotherapeutic

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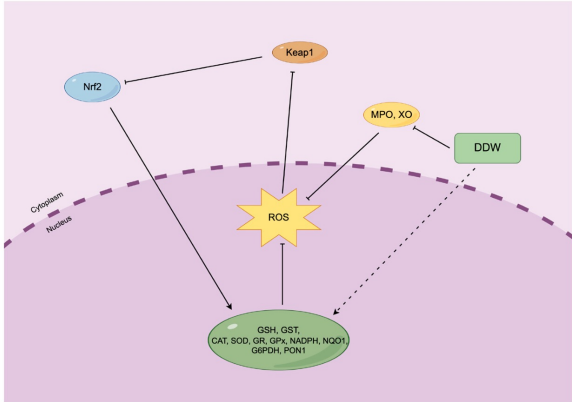


Figure 2. Schematic representation of the Keap1-Nrf2 signalling pathway for gene expression control. (By Figdraw). Excess ROS induces the suppression of Keap1, further disassociating Nrf2 from Keap1 to enter the nucleus. Accumulation of Nrf2 in the cellular nucleus causes antioxidative gene expression, suppressing ROS production. Additionally, DDW controls the expression level of antioxidative genes and inhibits the oxidative genes.

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Deuterium-depleted water stimulates GLUT4 translocation in the presence of insulin, which leads to decreased blood glucose concentration

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Abstract
Deuterium (D) is a stable isotope of hydrogen (H) with a mass number of 2. It is present in natural waters in the form of HDO, at a concentration of 16.8 mmol/L, equivalent to 150 ppm. In a phase II clinical study, deuterium depletion reduced fasting glucose concentration and insulin resistance. In this study, we tested the effect of subnormal D-concentration on glucose metabolism in a streptozotocin (STZ)-induced diabetic rat model. Animals were randomly distributed into nine groups to test the effect of D₂O (in a range of 25–150 ppm) on glucose metabolism in diabetic animals with or without insulin treatment. Serum glucose, fructose amine-, HbA1c, insulin and urine glucose levels were monitored, respectively. After the 8-week treatment, membrane-associated GLUT4 fractions from the soleus muscle were estimated by Western blot technique. Our results indicate that, in the presence of insulin, deuterium depletion markedly reduced serum levels of glucose, -fructose amine, and -HbA1c, in a dose-dependent manner. The optimal concentration of deuterium was between 125 and 140 ppm. After a 4-week period of deuterium depletion, the highest membrane-associated GLUT4 content was detected at 125 ppm. These data suggest that deuterium depletion dose-dependently enhances the effect of insulin on GLUT4 translocation and

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Table 3. Effect of deuterium content of drinking water on the metabolic parameters of diabetic rats treated with insulin (twice 1 IU/300 g bw/day).

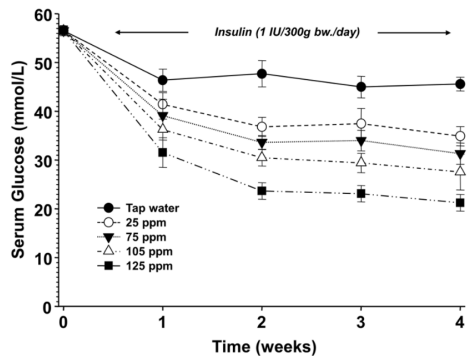


Fig. 2 The effect of deuterium content of drinking water on the serum glucose concentration in diabetic rats treated with insulin (twice 1 IU/300 g bw/day)

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THE LOW DEUTERIUM FOOD LIST

LOWER IN DEUTERIUM (FAVOUR)	HIGHER IN DEUTERIUM (LIMIT)
Healthy fats & oils: coconut, olive, avocado	Sugar and all sweeteners
Grass-fed and fatty animal proteins	Grains: wheat, corn, rice, bread, pasta
Eggs and fatty fish	Starchy roots: potato, sweet potato
Non-starchy green & leafy vegetables	Sweet fruits: especially tropical and dried
Nuts and seeds (in moderation)	Legumes and most processed carbohydrates

<https://yavelle.com.au/blogs/news/low-deuterium-food-list>
<https://yavelle.com.au/>

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Natural Factors Influencing Deuterium

- If you are looking to explore deuterium levels without buying expensive specialty water, researchers point out that the human body naturally generates its own deuterium-depleted water (metabolic water) through certain lifestyle factors:
- To lower deuterium in your body, prioritize a ketogenic-style diet rich in healthy fats, minimize high-carbohydrate and processed foods, and consume Deuterium-Depleted Water (DDW). *Fat metabolism produces metabolic water that is naturally lower in deuterium, which enhances mitochondrial efficiency and energy production.*
- Food Choices: Green leafy vegetables and animal fats are naturally lower in deuterium, while *simple starches, sugars, and equatorial fruits tend to store higher amounts of heavy hydrogen.*
- Natural Geography: Glacial runoff and cold mountain spring waters naturally feature slightly lower deuterium concentrations than coastal seawater or surface water near the equator.
- *Choose Fats & Greens: Emphasize healthy fats (e.g., olive oil, avocado, butter, grass-fed tallow), quality proteins, and organic leafy greens.*
- *Limit Carbs & Sugars: Reduce intake of grains, potatoes, and high-sugar fruits, as carbohydrates tend to carry higher deuterium levels.*

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Deuterium Depleted Water and Health

Natural Factors Influencing Deuterium

- **Eat Younger Foods:** According to deuterium-depletion protocols, young plants and meats from grass-fed, young animals have lower deuterium levels than their mature counterparts. []
- **Intermittent Fasting:** Fasting shifts your body from burning glucose to burning fat, producing deuterium-depleted water naturally.
- **Exercise:** Regular physical activity and sweating promote fat oxidation, which further aids the production of metabolic water.
- **Light Exposure:** Morning sunlight exposure and red light therapy are thought to support mitochondrial function and optimize cellular hydrogen processing.
- **Cold Exposure:** Practices like cold plunges or cold showers are believed to increase metabolic heat production and assist in deuterium reduction.
- For a more structured approach, you can explore commercial Deuterium-Depleted Water (DDW) programs to substitute regular tap or bottled water.