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Nutritional Deuterium Depletion and Health: A Scoping Review

Nicole Korchinsky
Nova Southeastern University, nicolekorchinsky@gmail.com

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Nicole Korchinsky

Nova Southeastern University

Dr. Kiran C. Patel College of Osteopathic Medicine

Department of Nutrition

NUT 6805 – Applied Nutrition Capstone

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Abstract

Background: Deuterium depletion is an untapped area of energy metabolism and health.

Objectives: The purpose of this scoping review is to examine the health effects through deuterium depletion via deuterium-depleted water and a deuterium-depleted diet (ketogenic).

Methods: A protocol process approach was used to retrieve current research in deuterium depletion.

Results: 15 research articles were used. 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.

Conclusion: Even with limited data, consistent deuterium depletion was seen across all conditions reviewed. More randomized control trials are recommended to confirm cause and effect.

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Introduction

Nutrition, if anything, profoundly affects our health. There is so much nutrition information everywhere that it is hard to find reliable guiding principles based on paramount components rooted in medical biochemistry, mitochondrial substrate oxidation foundations, and cellular energy production. Mainstream puts a spotlight on the many facets of a diet, but there’s another spoke on the wheel that has potentially slipped under the radar that may have an impact on health – heavy hydrogen, i.e. deuterium. Deuterium content in water and food consumption is not a popular or even known topic. For these reasons, a scoping review was conducted to provide existing knowledge in the field and map the research done in this area.

The following research question was formulated: “Does nutritional deuterium depletion have an impact on health?”.

What is deuterium?

Hydrogen is an atom that has a naturally occurring stable isotope, called deuterium (D).[1] Hydrogen has one proton in its atomic nucleus, whereas deuterium has one proton and one neutron, giving it a mass number of 2.[1,2] Regarding stable isotopes of the same element, hydrogen and deuterium have the largest mass difference, which causes magnitude differences in physical and chemical properties.[1] In nature, the ratio of deuterium to hydrogen (D/H) ratio is about 1:6600; the natural concentration of deuterium and in the human body is about 150 ppm (parts per million) or 12 to 14 mmol/l.[3,4] Published in 1993 was the first paper illuminating that

reduced deuterium-concentration has an impact on living organisms.[3] There are many proposed mechanisms for this.

Mechanism

Deuteration (the process of introducing deuterium into a molecule or chemical compound) of ATPase, including both ATP synthase and ATP hydrolase, has devastating biological consequences.[2] ATP synthase is an inner mitochondrial enzyme complex to tunnel protons from the intermembrane compartment to the matrix (innermost confinement) of mitochondria.[2] It uses protonation (addition of a proton) to produce a wheel-like rotation to make ATP, which is the energy currency in living systems.[2] Partial deuteration of the H^+ system led to unequal protons, which destroys proton tunneling.[5] Increasing D/H ratio in the intracellular space has been shown to be a determinant in cell growth.[3] Deuterium is precisely regulated in biology via either depletion (deupletion) during mitochondrial citrate synthesis to protect rotary (moving) proteins such as ATPase nanomotors[2] or accumulation, on the other hand, in structural proteins such as bone collagen with adaptive impact.[6]

Scientific evidence of Deutenomics in peer reviewed medical literature

Deutenomics is the science of biological deuterium fractionation and discrimination.

From the above, natural fatty acid availability for peroxisomal, then complete mitochondrial oxidation, is considered an effective deupleting mechanism across various diseases with translational and clinical significance.[7] For example, metabolites from a study related to improved lung cancer patient survival are long chain fatty alcohols, which result from oxidative processing in peroxisomes or from dietary sources.[8] These are ketogenic substrates that

are lower in deuterium content (105 – 130 ppm).[8] When the mitochondria process ketogenic substrates, it leads to the making of metabolic/matrix water via beta-oxidation with relatively low deuterium.[8] Oppositely, pentose-cycle derived NADPH will have raised deuterium content and raised markers from these substrates are correlated with reduced survival.[8]

Defective mitochondria in renal cell carcinoma can dictate tumor transformation by deuterium oncoisotope accumulation.[9] Thus, extracellular deuterium depletion acts as a metabolic therapeutic adjuvant and deupletion can be introduced by diet and drinks.[9,10,11]

Recent studies indicate diet as the main source of increased fatty acid pool in plasma; thus, production of ketones using these deuterium-depleted fatty acids might illustrate the benefit of ketogenic diets.[12]

This study reiterates the importance of inadequate mitochondrial deuterium depletion, resulting in oncogenic transformation in colon cells via metabolic profiling.[13]

Regarding the scientific information and evidence available on Deutenomics in peer reviewed medical literature, there is justification for a review.

Deuterium Depletion

How much deuterium will be in your cells depends on a number of things. Firstly, the deuterium concentration of fluid intake (including water from food).[4] Secondly, deuterium concentration of nutrient molecules because after oxidation of carbohydrates, proteins, and fats by the mitochondria, metabolic water is produced with decreasing deuterium content, in the same order.[4] Oxidation of glucose produces metabolic water with higher deuterium level.[4] A carbohydrate-rich diet will lead to the production of metabolic water with a deuterium

concentration around 155.75 ppm.[4] When the mitochondria oxidize fats/lipids, it produces metabolic water with as low as 118 ppm deuterium concentration.[4]

Deuterium depletion can be also acquired in living organisms through the consumption of deuterium-depleted water (DDW).[14] In regular bottled water, deuterium concentration is usually between 135 and 158 ppm.[14] Consuming 1.5-2 L of DDW with 105 ppm deuterium content day by day resulted in an inner deuterium level decrease of about 1 ppm per day.[15] The continued use of DDW with the same deuterium level led to an equilibrium.[15]

Deuterium depletion can also be attained through eating a lower deuterium content diet.[16] Grass-fed (ketogenic) animals showed a lower deuterium content (<130 ppm).[16] Artificially mixed grain-fed (metabolically glycogenic) animals had higher deuterium content (>140 ppm).[16] In dairy cows, the interference of the deuterium-depletion process leads to the burning of high deuterium nutritional products into metabolic water upon oxidation in the human body; this could contribute to the same metabolic conditions and diseases for humans that it had for cows.[16] Grain feeding usually includes the use of glyphosate herbicide in genetically modified crops; this limits oxygen delivery to mitochondria for efficient deuterium-depleted metabolic water production.[16] Glyphosate contaminated grain feeding of dairy cows presents odd-chain fatty acids with branched chain amino acids into metabolism by way of the tricarboxylic acid (TCA) cycle and disturbs mitochondrial proton tunneling because of the high deuterium metabolic water production with health compromising effects in the human consumer.[16] This study's results suggest that high deuterium content of processed dairy products that come from grain-fed cattle, as a significant contributing factor to degenerative and metabolic disease conditions (like obesity, diabetes, cancer, and Alzheimer's).[16]

Aim of this scoping review

The purpose of this scoping review is to examine deuterium depletion through deuterium-depleted water and a deuterium-depleted diet (natural ketosis) and possible health effects.

Methods

A scoping review was the most appropriate method due to the rationale that this is an emerging topic. This scoping review followed the PRISMA-ScR[17] for scoping review checklist (Figure 1). Data extraction table was created and entered by one researcher (Table 1). The inclusion criteria included original research identifying nutritional deuterium depletion and health. Exclusion criteria included secondary and tertiary sources. All study designs included human and animal data. The inclusion dates were 2008 until the present time 2024 and written in English. Search engines used were: PubMed, Wiley, Elsevier, and ResearchGate. Evidence search terms included: deuterium, deuterium depletion, deuterium depleted water, deuterium content, deuterium-depleted water, effects of deuterium depletion, deuterium depleting nutritional ketosis, deuterium depleted water effects, deuterium level, deuterium concentration. Articles that were highly relevant to the topic and matched the research question were selected. The PRISMA Scoping Review Checklist was used.

I used an expert in the field, Dr. Laszlo G Boros, to further add articles on this topic. This expert was also used in consultation. In addition, I was provided with more articles from another expert in the field, Dr. Gábor Somlyai.

Results

Study disposition

In this scoping review, 17 studies were identified addressing deuterium depletion and health research across various study designs published between 2008 and 2024. Two papers were excluded due to lack of full English translation. There were no duplicate articles. As a result, 15 articles are included in this review. Data extraction provided in appendices (Table 1).

Themes

All retrieved articles were heterogenous in nature. Themes did not evolve. Below describes data in the health categories.

Cancer

Studies have confirmed the role of deuterium in prevention of cancer development:

Kovács et al., In mice that were exposed to chemical carcinogen, the survival data after one-year showed that drinking deuterium-depleted water (30 ppm) prevented tumor development.[18] 97.3% of genes were upregulated when the deuterium concentration in media was higher-than-normal (300ppm).[18]

Kovács et al., showed that blocking the increase of intracellular deuterium concentration prevents the expression of cancer-related genes, tumor development, and tumor recurrence in cancer patients.[18] In 204 cancer patients with remission, who drank deuterium depleted water, 77.9% did not relapse, while 8 out of 11 deaths happened after stopping drinking deuterium depleted water.[18] The proposed mechanism is preventing the D/H ratios (through drinking

deuterium-depleted water) to reach the threshold necessary for cell division; suggesting that this could be a solution to reducing the relapse rate of cancer in patients and/or decreasing the cancer incidence in healthy people.[18]

Many studies proved the anticancer effect of deuterium depletion:

Somlyai et al., showed that when laying hens' normal drinking water was replaced with deuterium-depleted water (25 ppm), the deuterium level of the albumen in their egg decreased from 160 ppm to 110 ppm in 42 days and decreased of deuterium content of yolk; proving the influence it has on the body.[4] In two in vivo mouse models: one model 4T1 cell line with high metastatic capacity to lung showed deuterium depleted water and/or deuterium depleted yolk led to smaller tumor volume.[4] In the group treated with deuterium-depleted yolk there was a significant difference in smaller tumor weight ($p = 0.0354$).[4] The decrease in metastasis suggests that deuterium depletion may inhibit migration.[4] Mice transplanted with an MCF-7 breast cancer cell line showed that the anticancer effect of deuterium depleted water was enhanced by yolk containing deuterium-depletion.[4]

Cong et al., determined that deuterium depleted water has been shown to inhibit lung tumor growth in vivo as well as inhibited the proliferation of A549 cell lines with an accompanying increase in apoptosis.[19] Tumor weight was decreased.[19] In the deuterium-depleted water group, tumor inhabitation rate was 30%.[19] In A549 cells treated with deuterium-depleted water (50 ppm), the increase in apoptosis formation was significant ($P<0.05$).[19]

Kovács et al.: human, double-blind, randomized, 4-month long, phase II, placebo controlled, clinical trial showed that deuterium depletion delays the progression of prostate cancer.[1] In the prospective trial, in the treated group (deuterium-depleted water at 85 ppm) versus

placebo group (normal water at 150 ppm), they achieved the following: partial response ($p = 0.046$), net decrease in prostate volume was three times higher ($p=0.0019$), urination complaints stopped at a higher rate ($p = 0.0041$), and one-year survival rate was higher ($p = 0.034$).[1]

Krempels et al.: human, case-based, retrospective evaluation showed deuterium depletion in addition to conventional treatments, improves mean survival in lung cancer.[20] In the four patients consuming deuterium-depleted water survival time was 26.6, 54.6, 21.9, and 33.4 months, respectively, which is unique in the records of brain metastases from lung tumors.[20]

Somlyai et al.: human, preliminary study showed deuterium depletion in combination with conventional therapy, improved median survival time of Glioblastoma Multiforme patients.[15] The patients who drank deuterium-depleted water (85, 65, 45, and 25 ppm) had a longer median survival time (30 months) compared to the historical control (12.1-14.6 months).[15]

Krempels et al.: human, retrospective study showed deuterium depleted water in combination with or as an extension of conventional therapies, prolonged median survival time in certain subgroups of breast cancer patients.[21] Deuterium-depleted water (65-105 ppm) versus normal water (150 ppm) prolonged median survival time in comparison with published data.[21]

Gyöngyi et al.: in a clinical study in 129 patients with small cell and non-small cell lung cancers who drank deuterium-depleted drinking water in addition to conventional chemotherapy and radiotherapy, median survival time was 25.9 months in males and 74.1 month in female patients; this was statically significant ($p < 0.05$).[14] For women with tumors overexpressing cancer-related genes, those who drank deuterium-depleted water had a median survival time that was 2 – 4 times longer than what is typically seen in lung cancer patients.[14] Gyöngyi et al., also did a study of gene expression analysis in mouse lung indicated that deuterium-depleted water

attenuates 7,12-dimethylbenz(a)anthracene (DMBA) induced expression of Bcl2, Kras, and Myc in females.[14]

Boros et al,: human, pancreatic adenocarcinoma patients were treated with conventional chemotherapy and deuterium-depleted water (at 85 ppm DDW then gradually decreased to preparations with 65 ppm and 45 ppm deuterium content for each 1 to 3 months treatment period). "The mean survival time for patients consuming DDW treatment (n = 56) was 19.6 months in comparison with the 6.36 months' MS achieved with chemotherapy alone (n = 30). There was a strong, statistically significant Pearson correlation ($r = 0.504$, $p < 0.001$) between survival time and length and frequency of DDW treatment."[22]

Depression

Strekalova et al., in mice, substitution of normal drinking water with deuterium-depleted water (91ppm) counteracted the depressive-like state.[23]

Strekalova et al., epidemiological study showed a significant positive correlation between geographical distribution of the deuterium content of natural tap water in the US population and rates of depression.[23] There was a significant correlation ($p = 0.0016$) between deuterium content of tap water and rates of depression.[23] From the data it was estimated that the prevalence of depression is increased 1.8% for every 10 ppm increased in deuterium of the tap water ($p = 0.0016$).[23] "Deuterium content of drinking/cooking water affects chronic mental disease susceptibility.[23]

Diabetes (Metabolic regulations)

Molnár et al., confirmed that deuterium depletion, in a dose-dependent manner, enhanced the effect of insulin on Glucose Transporter type 4 (GLUT4) translocation.[24] In diabetic rats, it potentiated glucose uptake, which led to lower serum glucose, fructose amine, and HbA1c concentrations.[24] An animal study of rats, showed that the optimal deuterium concentration of blood for reducing blood sugar levels was 125 and 140 ppm.[24]

Somlyai et al., clinical prospective study of human volunteers with pre- or manifest diabetes, DDW (104 ppm) significantly decreased the fasting glucose level and reduced insulin resistance.[25]

Promising New Areas

Long Term Memory

Mladin et al., found in normal rats, deuterium-depleted water (27-30 ppm) in comparison to normal water (145-150 ppm) significantly decreased the number of reference memory errors, speculating that DDW may stimulated long-term memory.[26]

Anti-aging

Avila et al., showed that in *Caenorhabditis elegans* (*C. elegans*) [nematode][worms], DDW (90 ppm) reversed manganese (Mn)-induced lifespan decrease, restoring lifespan.[27]

Sports Performance

Boros et al., in a report, after six failed attempts by the same high altitude professional mountain climber using carbohydrate-based nutrition (glycogenic), the athlete in deuterium

depleting nutritional ketosis was finally able to summit Mount Everest without supplemental oxygen.[7]

Discussion

To summarize the main findings, deuterium possesses profound biological effects, and deuterium depletion has major roles for example: in the prevention of cancer development with various anticancer effects, it lowers the rates of depression, reduces circulating glucose in diabetes, stimulates long-term memory, increases lifespan, and enhances sport performance.

The findings from animal studies indicate that deuterium depletion prevented tumor development, prevented the expression of cancer-related genes, as well as preventing tumor development. This data further highlights smaller tumor volume and smaller tumor weight. Additionally, deuterium depletion shows a counteraction of a depressive-like state. Findings also show reduction in blood glucose levels. Deuterium depletion in mice simulated improved long-term memory. Anti-aging was demonstrated.

Deuterium depletion in humans showed delayed progression of prostate cancer. Deuterium depletion also showed improved mean survival time in lung cancer, Glioblastoma Multiforme, certain subgroups of breast cancer patients, small cell and non-small cell lung cancers, and advanced pancreatic cancer. In addition, deuterium depletion was associated with absence of relapse in cancer patients. Furthermore, fasting glucose levels and reduced insulin levels were found in deuterium depleted individuals with pre or manifest diabetes. Increase in sports performance was also exhibited.

This scoping review has some limitations. Some of the studies included were in vivo, in vitro, and animal models; this can be difficult to translate these outcomes into humans. Also, the findings indicate a majority of research focusing on cancer. Furthermore, this scoping review’s results are from a small number of studies and only one randomized controlled trial, which limits the ability to confirm cause and effect. There was limited information available on anti-aging, therefore at this time, any evidence is lacking, and more research is needed. Although there was one study available on sports performance, this area is promising. There is abundant space for further research to establish more about deuterium depletion and its effect on human health.

Conclusion

Due the limited information currently available on deuterium, existing knowledge in the field and mapping of research was done in this area. Overall, the data analysis supports that deuterium depletion through deuterium-depleted water and a deuterium-depleted diet (ketogenic) has an impact on health. Therefore, this review examined the evidence regarding nutritional deuterium depletion related to the results of cancer prevention, cancer treatment, depression, diabetes, long-term memory, anti-aging, and sports performance and concluded a positive impact. The positive results were consistent, even with limited number of studies and study designs currently available. It can be concluded that nutritional deuterium depletion can and should be proposed for future studies and high-quality research priorities, especially in more human studies, to determine further.

Author Contributions / Acknowledgments

The review was conceptualized by Nicole Korchinsky. Searches, screening and extraction have been conducted by Nicole Korchinsky and Dr. László Boros. Nicole Korchinsky, Dr. László Boros, and Dr. Anne M. Davis reviewed and discussed the results. Nicole Korchinsky, Dr. László Boros, and Dr. Anne M. Davis contributed to the manuscript and approved the final version.

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Conflict of Interest

The author(s) declare that there is no conflict of interest.

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Appendices

Figure 1 - PRISMA-ScR Checklist

Table 1 – Data Collection and Review Results