Deuteronation and Aging

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ABSTRACT: Deuterium has one proton and one neutron in its atomic nucleus, but hydrogen has only proton. The natural abundance of deuterium is 1 per ∼6600 hydrogen atoms. Therefore deuterated water (both HOD + D_2O [heavy water]) abundance is 1 per ∼3300 water molecules. One dissociation product of deuterated and heavy water is deuteron (proton + neutron, D^+, H_2OD^+/D_3O^+). Because heavy water has a lower ionization constant than water, the D^+/H^+ ratio is ∼1/15,000 in biological fluids. O-D bond length is shorter than O-H, and D-O-D angle is lesser than H-O-H. Once a deuteron exchanges with proton on the water-exposed surface of a macromolecule, it can lead to a conformational change and the reverse exchange will be less likely. Deuteron bonds are stronger than proton bonds. Therefore an increase of deuteronated macromolecules can be expected in due course of time. In order to test this hypothesis, we conducted a pilot study and measured the D/H ratio in the tails of three Sprague–Dawley rats at different ages (4 weeks, 5 weeks, and >1-year old) by elemental analysis coupled with isotope ratio mass spectrometry (EA-IRMS) technique. To prevent the effect of daily water consumption, the homogenized tails were lyophilized before analysis. The results, as mean of several measurements, of 4 weeks, 5 weeks, and >1-year-old rats were ‰–94 ± 9.56, ‰–101.71 ± 6.89, ‰–83.68 ± 3.46 $\delta(^2H)$ relative to VSMOW, respectively. Although there is a slight increase in >1-year-old rat, the difference among the animals was not significant. We propose that, before reaching to a final conclusion about the accumulation of deuterium with aging, the measurements should be done not in whole tissue samples but in purified macromolecules from a larger set of animals.

KEYWORDS: deuteronation; aging; heavy water

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INTRODUCTION

In nature, there is one deuterium (D) atom per ∼6600 hydrogen (H) atoms.[1] Deuterium has one neutron and proton in its atomic nucleus, but hydrogen has only proton (FIG. 1). Deuteron (D^+) is the chemical name for deuterium without electron, as proton (H^+) for hydrogen. The forms of water (H_2O) having deuterium are deuterated water (HOD) and heavy water (D_2O). The abundance of deuterated + heavy water is one per ∼3300 water molecules. The dissociation products of water are $H^+/(H_3O^+)$ and OH^-. The ionization of deuterated and heavy water generates $D^+/(H_2OD^+, D_3O^+)$ and OH^-. The ionization constant of water (1.008×10^{-14}, pH = 6.99) is 5.17-fold higher than heavy water (1.95×10^{-15}, pD = 7.35).[2] Therefore, the ratio of deuteron to proton is 1/(6600 × 2.27), which is equal to ∼1/15,000. We can conclude that in any process of protonation, the chance for deuteronation is ∼1/15,000. Chemical bond properties of deuterium are different than hydrogen. For an isolated molecule, calculated O-D bond length (0.957835 Å) is shorter than O-H (0.957854 Å), and D-O-D angle (104.490°) is lesser than H-O-H (104.500°).[3] For liquid water, experimental results obtained by neutron diffraction studies show greater values (O-H length 0.970 Å, H-O-H angle 106°).[4]

Inside the cells, there is a continuous exchange of protons on the water-exposed surfaces of macromolecules. During this exchange, a deuteron can replace proton. Since deuteron makes a stronger bond, it will be very less likely to replace the deuteron with proton. Therefore, it can be suggested that a time-dependent increase of deuteronation of especially long-living macromolecules is likely. If such an increase exists, this can contribute to the mechanisms of aging, by leading to some conformational changes in functionally important structural sites of macromolecules.[5]

In this pilot study, we analyzed tail tissue deuterium levels in young and aged rats in order to detect any age-dependent change in the deuterium/hydrogen ratio.

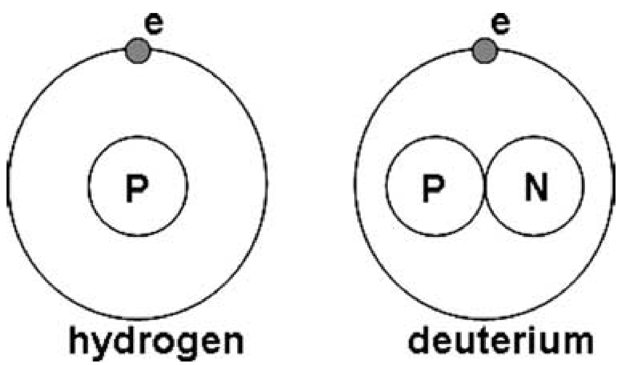

FIGURE 1. The atomic structures of hydrogen and deuterium.

EXPERIMENTAL METHODS

In this study, a total of three Sprague–Dawley rats (obtained from Gülhane Military Medical Academy Research Center Animal Facility) at the ages of 4 weeks, 5 weeks, and >1-year old were used. A small part of tail tips were excised by standard procedure. Tails were mortar homogenized in liquid nitrogen. Homogenized tissues were then lyophilized in order to remove all water molecules that can effect measurements by the deuterium composition of daily water intake. The measurements were performed in Stable Isotope Laboratory of Turkish Petroleum Corporation Research Center Geochemistry Department, by elemental analysis coupled with isotope ratio mass spectrometry (EA-IRMS) using the standard technique, which is quite labor-intensive. Each sample was measured 3–9 times. The results were reported as means of several measurements as "‰– value δ(2H) relative to VSMOW" (Standard Mean Ocean Water). The results have negative (–) values.

RESULTS AND DISCUSSION

Deuterium levels of rat-tail tissue samples were given in TABLE 1. As can be concluded from the data, although there is a slight increase in >1-year-old rat, there was not a very significant difference among the animals. If this slight increase depends on the increase of deuteronated long-living macromolecules that compose only a certain fraction of whole-tail tissue sample, this result could be meaningful. But it is obligatory to analyze deuterium levels in purified long-living macromolecules before a final conclusion. We had to use a very small number of animals due to technical constraints in

TABLE 1. Deuterium levels of tail tissues from three Sprague–Dawley rats at different ages

Deuterium levels (as ‰– (^{2}H) relative to VSMOW)	Animals (age)		
	4 weeks	5 weeks	>1 year
All measured values from each sample	−85.23	−96.09	
	−82.69	−92.74	
	−88.96	−103.82	−85.6
	−84.39	−99.01	−79.68
	−97.59	−100.97	−85.77
	−100.97	−99.63	
	−92.12	−106.22	
	−105.44	−115.26	
	−108.61		
Mean ± SD	−94 ± 9.56	−101.71 ± 6.89	−83.68 ± 3.46

this pilot study. A larger set of animals will be used in the forthcoming studies.

Although the natural abundance of deuterium is very low, we should keep in mind the very high concentrations of water in biological systems. Therefore, the concentration of deuterium is not negligible. We propose that the stochastic biological consequences of natural deuterium abundance need to be investigated in the future.

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