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D/H control of chemical kinetics in water solutions under low deuterium concentrations

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Highlights
- Deuterium depletion
- Kinetic isotope effect
- Biochirality

1. Introduction

Natural water represents a multicomponent mixture of molecules of different isotope composition (isotopologues). In natural water one million molecules on average includes 997284 molecules of $^1H_2^{16}O$, 311 molecules of $^1H^2D^{16}O$, 390 molecules of $^1H_2^{17}O$, and about 2005 molecules of $^1H_2^{18}O$. The concentration of water molecules containing deuterium (D) in natural waters fluctuates within the limits established in two basic international standards for the isotope composition of hydrosphere: VSMOW (Vienna Standard Mean Ocean Water) and SLAP (Standard Light Antarctic Precipitation) introduced by the International Atomic Energy Agency (IAEA) [1]. In accordance with the VSMOW standard the absolute contents of deuterium $^2D/^1H$ in the ocean water amount to 155.76 ± 0.05 ppm. The SLAP standard characterizes the lightest natural water on Earth with at D/H = 89 ppm. Deuterium depleted water – ddw - (from SLAP deuterium content to ratio D/H = 5 ppm) has a number unexpected biological features, including antitumor [2], antidote [3] and metabolic effects [4]. The 2-3-times kinetic isotopic effect due to full changing of H by D is very well known. In the report we investigated the kinetic isotopic under the increasing of deuterium concentration from 0,5 mM (D/H ratio near 5 ppm) to 16 mM (corresponding to European water's D/H ratio near 140 ppm) for different processes (galactose mutarotation, dissolving of solid compounds, the enzyme reaction with polymer substrate, cell transition of the biosensor). Chosen processes illustrate the unexpected increasing of reaction rates under low concentrations of deuterium changing comparably or more with well-known effects of full D/H substitution.

2. Methods

The content of deuterium and oxygen-18 was controlled by using the multiple-pass laser absorption spectroscopy with an LWIA-24d instrument produced by Los Gatos Research, Inc.

Rotation angles of plane-polarized light were measured using an Atago POL-1/2 automated polarimeter (Japan). The accuracy of the measurements was $\pm$ 0.002° for angles <1° and $\pm$ 0.2% of the indicated value for those >1° [5].

Kinetic control of dissolving of solid state of lactose and bendazole provided by Low Angle Laser Light Scattering (LALLS, Malvern Instruments) by control of time curve of obscuration (1-T) caused by nondissolved dispersed particles [6].

The lysozyme activity of the enzyme destabilase-lysozyme was determined by the nephelometric method with the suspension of the cell walls of the bacterium *Micrococcus lysodeikticus* [7].

Quasichemical kinetic of cell transition of cellular biosensor *Spirostomum ambigua* estimated by the time of cell transition and immobilization depend on deuterium concentration in water [8].

3. Results and discussion

We compiled the experimental results based on different level of organization of reaction systems: molecular, supramolecular, two-phase heterogenic, living cells.

3.1 Molecular level of organization of reaction mixture. For the D-galactose enantiomers there are the decreasing of rate constants for galactose mutarotation due to the increasing of deuterium contents (for 24 ^{o}C): 0,5 mM HOD – 16×10^{-5} c^{-1}, 16 mM HOD - 12×10^{-5} c^{-1}, D$_2$O - 8×10^{-5} c^{-1}. At low concentrations there is no difference in dependence of rate constants on temperatures whereas the dependence of activitaion energy on deuterium may occur only after full substituion of H for D. The mutarotation rate constant for the L-isomer was 2-times less than that for the D-isomer over the whole temperature range witouth depenedence on HOD concentration in low values. First-order mutarotation kinetics were not observed for L-galactose in heavy water.

3.2 **Supramolecular level - water solution of biopolymers.** The initial rate of lysozyme activity of destabilase-lysozyme two-fold increased then HOD decrease from 16 mM HOD to 0,5 mM HOD whereas the full substitution of protium for deuterium did not influence on initial rate.

3.3 **Level of water suspension - dispresed (two-phases) system.** The kinetic of dissolving of 80-μ powder of lactose demonstrated the 1.6 – 1.7 increasing of observed first-order rate constants (for bendazole-HCl – 1.8-2.1 depending on preparation) when the HOD decreased from 16 mM HOD to 0,5 mM HOD. The k$_H$/k$_D$ ration (relation of rate constants for 16 mM HOD and D$_2$O, respectively) was 1.6.

3.4. **Living cell's level.** The rate of cell death of free living in bulk water infusoria *S. ambigua* is strongly depended on D/H ratio. The increasing of rate constant for the processes of irreversible cell transition (from an active state to an immobilized state) was up to 800 times under deuterium depletion from 16 mM to 0,5 mM. The curve of life time of cell biosensors has the plateau between value of D/H from 90 ppm to 150 ppm with two declines forward to values of D/H = 5 ppm and 99% deuterium oxide [8]. Such dramatic kinetic isotope effect is in agreement with similar data for multisteps enzyme reaction catalyzed by succinate oxidase in mitochondria [9]. The nature of such colossal "inhibiton" of enzymes cascades (from mitochondria to hole cell and organism) by deuterium may consists in participation of heave isotope of hydrogen in realization of chirality processes. There is the demonstration of the coupling between chirality and isotopes effect for galactose mutarotation. The demonstrated isotopes' effects may be use for thin regulation of pharmacokinetics of drugs with simple using only deuterium depleted water.

4. Conclusions

There is the kinetic isotope effect for different reaction water solutions (including dispersed system) during changing of deuterium concentration from 0,6 mM (rate constant – k$_{ddw}$) to 16 mM (rate constant – k$_H$) comparably or more with well-known effects of full D/H substitution (rate constant – k$_D$). For molecular systems k$_{ddw}$/k$_H$ (like as k$_H$/k$_D$) is near 2, whereas for living cells k$_{ddw}$/k$_H$ is up to 800. Such dramatic effect may be connected with special role of deuterium in biochirality.

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Keywords
"deuterium depletion" "isotopic effect"