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REVIEW ARTICLE

The effects of physical treatment on physicochemical and biological properties of water and aqueous solutions

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Abstract

Objectives. *Changes to the properties of water caused by factors such as pressure or temperature, can only be explained by its structural changes. Scientists study changes to the properties of water due to various physical stimuli only without the addition of any substances. Examples of stimuli are acoustic exposure, thermal exposure, pressure variation, shaking, intensive vibration treatment followed by dilutions, vortexing, bubble generation, inter alia. The aim of the present review article is to summarize the available data on how the above processes affect the physicochemical and biological properties of water and aqueous solutions.*
Results. *It has been shown that heating makes water less compressible and decreases air solubility in water, while cooling enhances its viscosity. Acoustic exposure makes the structure of water become coarse-grained, followed by an increase the number of large clusters, pH and temperature inside a cavitation bubble. High pressure enhances the viscosity, self-diffusion, and compressibility of water. For bubble processed water, there are changes in the spin-spin and spin-lattice relaxation times. Reactive oxygen species are formed, as well as increased solubility of gases in liquids and reduced friction. Vortex process technology causes an increase of electrical conductivity of water and reduced viscosity. Intensive vibration treatment and dilution processes result in changes in electrical conductivity of water, dissolved gas*

concentration, ultrasonic wave velocity, pH, surface tension, dielectric constant, and spectral response. There is also data to support the biological effects of different types of physical treatment of solutions.

Conclusions. *This review shows that physical treatment of water can induce changes both in physicochemical and biological properties of water and aqueous solutions.*

Keywords: *water technology, water properties, mechanical treatment, aqueous solution*

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ОБЗОРНАЯ СТАТЬЯ

Влияние физической обработки на физико-химические и биологические свойства воды и водных растворов

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Аннотация

Цели. *Изменения свойств воды, вызванные различными факторами, такими как давление или температура, могут объясняться только структурными изменениями воды. Ученые исследуют изменения свойств воды, происходящие исключительно из-за различных физических раздражителей и без добавления каких-либо веществ. Примерами таких раздражителей являются акустическое и тепловое воздействие, изменение давления, встряхивание, интенсивная вибрационная обработка с последующим разведением, вихревое перемешивание, образование пузырьков и т.д. Целью данного обзора является обобщение имеющихся данных о том, как вышеуказанные процессы влияют на физико-химические и биологические свойства воды и водных растворов.*

Результаты. *Показано, что нагрев делает воду менее сжимаемой и снижает растворимость воздуха в воде, а охлаждение повышает ее вязкость. Акустическое воздействие приводит к тому, что структура воды становится крупнозернистой, что сопровождается увеличением количества крупных кластеров, pH и температуры внутри кавитационного пузыря. Высокое давление способствует увеличению таких физических свойств воды, как вязкость, самодиффузия и сжимаемость. Для воды, обработанной пузырьками, происходят изменения времен спин-спиновой и спин-решеточной релаксации, образуются активные формы кислорода, а также наблюдается повышенная растворимость газов в жидкостях наряду со снижением вязкости. Вихревой технологический процесс приводит к увеличению электропроводности воды и снижению* *вязкости. Интенсивная вибрационная обработка и процессы разбавления приводят к изменению некоторых характеристик воды, таких как электропроводность, концентрация растворенного газа, скорость ультразвуковой волны, pH, поверхностное натяжение, диэлектрическая проницаемость и спектральный отклик. В работе также представлены данные, подтверждающие биологические эффекты различных типов упомянутой физической обработки растворов.*

Выводы. *Данный обзор показывает, что физическая обработка воды может вызывать изменения как физико-химических, так и биологических свойств воды и водных растворов.*

Ключевые слова: *физическая обработка, свойства воды, свойства водных растворов*

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INTRODUCTION

Water is a unique chemical compound which has no analogue in nature. Many of its properties are considered anomalous from the perspective of theoretical science. In a stationary state water is an open non-equilibrium system capable of accumulating additional free energy [1]. It has been demonstrated that external influence (optical, plasma, mechanical, etc.) can radically change the macroscopic properties of liquid solutions [2–10]. Many papers describing the unique properties and features of the structure of water have been published [11–16], so we would like to focus more on data supporting the emergence of new properties of water and aqueous solutions after their exposure to mechanical actions. The influence of mechanical treatment on the chemical properties of compounds has been studied for a long period of time and is currently undergoing a boom [17–20]. Nevertheless, scientists in the field of mechanochemistry mainly focus on changes in the structure of solid chemical compounds rather than the structure of water which is usually viewed, if at all, as a nominal solvent. However, when liquid water is affected by certain factors, such as pressure or temperature, changes in some of its properties can only be explained by structural changes of water [21].

With regard to the mechanical treatment of aqueous solutions, scientists and primarily physicists are thoroughly investigating the acquisition of new properties by water which can arise without the addition of any chemicals. They are exclusively due to various mechanical stimuli such as: acoustic exposure; thermal exposure; pressure variation; shaking, intensive vibration treatment followed by a dilution step; vortexing; bubble generation, etc. The aim of this review is not only to describe the available data on how the above processes affect the physicochemical properties of water, but also to assess influence on the biological effects of such aqueous solutions. We are also interested in topics concerning exposure of water and aqueous solutions to other physical stimuli, for example, exposure to electromagnetic fields. However, we intentionally omit them in this review as they are much more investigated to date [22–25].

FEATURES OF THE STRUCTURE OF WATER

Before discussing the properties of water which can be modified following mechanical treatment, it is important to gain an understanding of the special properties of initial untreated water. For this, the features of its structure need to be analyzed. Bernal's basic work [26] and further development of its ideas resulted in the creation of the so-called standard model for water representing the structure of water as a hydrogen-bonded network: loose but tight at the same time. These asymmetric properties were established by Bernal and Fowler after comparing the radius of a water molecule with its expected density, found to be markedly lower than the calculated value (1.0 instead of 1.8 g/cm^3). These results were confirmed by Meyer, Steward, and Amaldi using X-ray diffraction measurements of water [27–29].

At the present time, the current model of water can be described as follows:

1. The tetrahedral geometry of water molecules might be responsible for water's unusual properties [26]. Two hydrogen atoms form hydrogen bonds with oxygen responsible for water's unique properties [30–34]. However, the manifestation of the unique properties of water is explained by the formation of two additional acceptor hydrogen bonds. As a result, water has strong orientational interactions in addition to van der Waals attractions and repulsions.

2. This leads to cage-like structuring, not only in the solid phases (ices) but also even in liquid water. Liquid water is a mixture of two fluids: a low-density one and a high-density one [35].

3. Liquid water is a mixture of types of structure. It is the structure of water that gives water its macroscopic properties [36–40].

4. Liquid water tends to be more cohesive than other simple liquids. Owing to their structural arrangement, water molecules spontaneously associate with each other into a tetramer through hydrogen bonds. Although hydrogen bonds are much weaker than covalent bonds (they have energies of 4–13 kJ mol compared to approximately 418 kJ mol for a carbon-hydrogen covalent bond [41]), they contribute to the overall molecular energy due to their high number and fast formation [42].

The above model is rarely disputed nowadays, but there are still a few questions to be asked. Moreover, the growing number of new experimental facts raises even more questions. One of these questions concerns the stability of density inhomogeneities in water. The existence of density inhomogeneities (so called water structures and clusters) in liquid water is a well-recognized fact [43–45]. However, some specialists think that water structures may be long-lived [14, 43], while other scientists consider that the life time of water structures is determined by the hydrogen-bond jump time. This does not exceed a few picoseconds, or longer times, but comparable to the hydrogen-bond jump time [31, 46].

The jump time of hydrogen bonds and, therefore, individual water structural elements can indeed be several picoseconds. However, replacing one structural element with another one does not lead to the destruction of the whole structure, making it dynamic and long-lived at the same time. The existence of a dynamic self-replicating network of water molecules in liquid water was proposed in 1998 [47]. It was then independently confirmed by an X-ray diffraction study of water nanodroplets [48, 49].

Different cluster sizes have been experimentally studied and theoretically described to date: small clusters (dimers to decamers) and clusters formed by several dozen [45, 50, 51], or even hundreds of water molecules [52]. The existence of water octamer, a formation previously regarded as thermodynamically unstable, has been confirmed. The ^{1}H nuclear magnetic resonance (NMR) spectroscopy demonstrated that dynamic hydrogen bonding in the size-specific cluster ($n = 8$) is one of the features of the thermodynamically metastable water cluster formed in hydrophobic solvents [53]. However, even highly purified water can contain impurities or ions that form stable water structures around themselves [54, 55]. The structures generated can be transformed into low-density to high-density forms, bending but not damaging some of the hydrogen bonds. The sizes of these structures depend on the concentration of impurities, medium temperature and pH, etc. [56–59].

PHYSICOCHEMICAL PROPERTIES OF WATER

The model of water described in the previous section is characterized by properties well known in the scientific literature. Being loose but tight, water has relatively high values of surface tension, melting point, and boiling point. Water has density anomalies which are manifested in various ways. For example, ice floats on liquid water. In most other materials, the solid sinks in the liquid. This density anomaly is due to the fact that applying pressure melts solid water into a liquid, whereas applying pressure drives most liquids to freeze into a solid [60].

Polymorphism of a crystal structure is a well-known phenomenon. More than five such structures can be counted for carbon (diamond, graphite, graphene, fullerene, etc.). Most substances are characterized by only one or two solid phases, water has more than a dozen phases of its solid, ice [11]. Water is a polar molecule, so its liquid can dissolve polar and ionic solutes. Its thermodynamic signatures for dissolving non-polar molecules are different from those of most other solvents. In order to signify that difference, it has been given its own name: the hydrophobic effect. Nevertheless, water has a number of properties which are beyond any doubt. For instance, water changes its phase into a solid at low temperatures. When heat is added to solid water (ice), it melts to become a liquid. Further heating results in boiling: a phase transition from the liquid phase to the gas phase. Therefore, at this level, the pressure-temperature (*pT*) phase diagram of water, which shows these features, is similar to the phase diagrams of other materials. The main physicochemical properties of water are presented in Table.

Experiments have demonstrated that exposure of water to mechanical stress may change some of the properties listed in the table. Since the structure of water is responsible for its properties, most types of exposure are directed at the clustering of this structure (formation, destruction, and association), changing intermolecular distance and the nature of hydrogen bonding, as well as the formation and collapsing of bubbles, which may change some of the properties (for example, heat capacity, molar volume, coefficient of thermal expansion, coefficient of isothermal compressibility, air solubility in water, water expansion with increasing temperature, viscosity with decreasing temperature, etc.). Each type of exposure will be detailed in the next sections.

ACOUSTIC EXPOSURE

The ultrasound beam originates from mechanical oscillations with frequencies ranging from 15 kHz to 10 MHz, above the range of normal human hearing. Since the speed of sound in water is about 1500 $m{\cdot}s^{-1}$, the corresponding wavelengths of acoustic waves are within the range of 10 to ~0.01 cm, which usually exceeds the sizes of atoms or chemical bonds to a significant level. As an ultrasound wave travels through a liquid, local pressure fluctuations, variable in space and time, induce acoustic cavitation. The effects of ultrasound result from acoustic cavitation, associated with the formation, growth and collapse of bubbles in liquids. In these processes, the low energy density of the sound field is converted into high energy density inside and outside the collapsing bubble [61]. The energy accumulated during the growth of a bubble in the expansion phase is released as acoustic noise, shock waves, chemical reactions, or as light emission when the bubble collapses abruptly during the contraction phase [62]. Didenko's work shows that ultrasound causes the temperature inside a

Table. The main physicochemical properties of water (at 25 °C and 101.325 kPa, where applicable)

Characteristic	Value
Density	997.047013 $kg{\cdot}m^{-3}$
Dielectric constant	78.375218
Magnetic susceptibility	$-1.64{\cdot}10^{-10}$ $m^3{\cdot}mol^{-1}$
Electric conductivity	0.05501 $\mu S{\cdot}cm^{-1}$
Limiting ionic conductivity	
H^+	349.19 $S{\cdot}cm^2{\cdot}mol^{-1}$
OH^-	199.24 $S{\cdot}cm^2{\cdot}mol^{-1}$
Ionic mobility	
H^+	3.623 Å ~ 10^{-7} $m^2{\cdot}V^{-1}{\cdot}s^{-1}$
OH^-	2.064 Å ~ 10^{-7} $m^2{\cdot}V^{-1}{\cdot}s^{-1}$

Table. Continued

Characteristic	**Value**
Thermal conductivity	0.610 $W \cdot m^{-1} \cdot K^{-1}$
Speed of sound	1496.69922 $m \cdot s^{-1}$
Refractive index	1.33286 (λ = 589.26 nm)
pH	6.9976
pK_w	13.995
Surface tension	0.07198 $N \cdot m^{-1}$
Kinematic viscosity	$0.8935 \cdot 10^{-6}$ $m^2 \cdot s^{-1}$
Dynamic viscosity	0.8909 mPa·s
Bulk viscosity	2.47 mPa·s
Diffusion coefficient	0.2299 $Å^2 \cdot ps^{-1}$
Dipole moment	2.95 D (at 27°C)
Adiabatic compressibility	0.4477 GPa^{-1}
Isothermal compressibility	0.4599 GPa^{-1}
Expansion coefficient	0.000253$°C^{-1}$
Adiabatic elasticity	2.44 GPa
Joule–Thomson coefficient	0.214 $K \cdot MPa^{-1}$
Vapor pressure	3.165 kPa
Cryoscopic constant	1.8597 $K \cdot kg \cdot mol^{-1}$
Ebullioscopic constant	0.5129 $K \cdot kg \cdot mol^{-1}$
Polarizability	$1.636 \cdot 10^{-40}$ $F \cdot m^2$

Note: Data collected from Chaplin M. *Water Structure and Science;* 2016. http://www1.lsbu.ac.uk/water/ (accessed June 29, 2020).

bubble to increase dramatically. The effective emission temperature during cavitation in water was measured to be 4027 ± 73°C (4300 ± 200 K) [62]. Ultrasound waves move through the solution as a result of several physical phenomena, such as micro-turbulence, micro-streaming, micro-jets and sound (or shock) waves. In this way they enhance the contact area and mass transfer between both media through cavitation process [63]. Therefore, ultrasonic irradiation may improve water purification. For example, an ultrasonic-assisted method was found to have advantages over shaking in terms of Pb^{2+} extraction from water. The extraction recovery of Pb^{2+} was enhanced by ≥2%, with a 7.5-fold shorter extraction time achieved, when compared to a thermostatic electrical shaker [64].

Kovalenko *et al*. [65] demonstrated that sound waves influenced the structural properties of water using a light-scattering method. It was shown that infrasonic waves of certain frequencies (5 and 10 Hz) destroyed clusters of less than 1.6 μm considerably. On the other hand, normal sound and ultrasound waves decreased the concentration of medium and small clusters with a radius of less than 0.9 μm and promoted the formation of extremely large clusters (≥3 μm). Thus, exposure to acoustic waves makes the structure of water coarse-grained. The increasing intensity of the affecting wave enhances damaging effects. As predicted by the authors, the number of extremely large clusters may also grow. This is due to the increased probability that the spatial relationship of clusters of various sizes will become optimal for the multiple occurrences of hydrogen bonds between them [65].

When water is exposed to long sound waves at the operating frequencies of the cavitator, the distance between clusters exceeds the acceptable limits at a certain moment. As a result, the interaction forces diminish and the liquid ‘breaks’. Later, the broken clusters will form clusters again, but with a different structure. There are several possible outcomes for this process:

1) a cluster may dissociate either into several fragments or into molecules;

2) the initial cluster may transform into another cluster and completely change its structure and shape (plane or spatial);

3) the structure of a cluster may be partially changed, with defects in configuration observed (for example, only from rigid deformation induced by the shock-wave front);

4) combinations of water molecules may appear due to hydrogen bonding with other molecules of the oxide group, with similar structures forming, but with a different composition, i.e., they are composed of the molecules of substances resulting from the destructive action of cavitation of solids;

5) water clusters may also be filled with molecules or fragments of other substances. It can have either more atomized or more integrated fragments. Clearly, changes to the shape and position of clusters can lead to changes in the properties of water when exposed to sound waves [66].

Thus, from the physical perspective, ultrasonic treatment increases the number of large clusters in water and the pH level. Intensive exposure to ultrasound causes cavitation that results in the formation of various free radicals and a temperature rise inside a cavitation bubble. This effect may be used for removing metal ions from water.

Water with changed properties can exert new effects on biological systems due to the transformation of its initial structure. Exposure of water to cavitation has been shown to enhance the germination capacity of seeds soaked in the exposed water when compared to untreated water [66]. Nevertheless, when biological systems themselves are exposed to ultrasound in an aqueous medium, this results in DNA damage, inhibition of enzyme activity, membrane damage, and cell death. This effect is caused by the generation of free radicals induced by ultrasound [61].

HEATING/COOLING

The presence of clusters in water can also be explained by temperature-dependent changes in its properties. When the temperature of distilled water and salt solutions rises to 40°C, clusters of 2 to 40 μm are destroyed, and energy absorption observed [57]. Water possesses characteristics of temperature dependence, such as heat capacity, molar volume, thermal expansion coefficient, isothermal compressibility coefficient, etc.

The heat capacity of water is relatively large, since water stores energy in both its van der Waals and hydrogen bonds. Water has a minimum volume at a temperature of maximum density, 4°C, whereas the volumes of simpler liquids increase monotonically. Cold water has a negative thermal expansion coefficient between 0 and 4°C; heating shrinks it. Further heating to 46°C makes water less compressible; while above 46°C water exhibits normal liquid behavior, in that as it heats up the compressibility increases [67].

The lifetime of molecular vibrations in excitation is expected to decrease with increasing temperature, while energy and the probability of interaction with other molecules also increase. For example, the lifetime of excited liquid HCl stretch vibrations decreases from 2.1 ns at −100°C to 1.0 ns at −25°C [68]. Excited OH-stretch vibrations in liquid water have a lifetime of 0.26 ps at 25°C, increasing to 0.32 ps at 85°C [69]. The increase in lifetime with temperature can be explained by the effects of the hydrogen bond network. OH-stretch vibrations usually become weaker through energy transfer to the overtone of the H–O–H bending mode. However, water hydrogen bonds are weakened with increasing temperature, resulting in high-frequency stretch vibrations and low-frequency bending vibrations. This increase in temperature gives rise to a shift of the overtone of the bending mode beyond the resonance with the stretching mode, making energy transfer less probable [69].

The solubility of air in water decreases as temperature increases: water contains less air at high temperature. For example, at 1 bar at 10°C city water will hold approximately 2.3% air by volume. If the water is heated to 91°C at the same pressure of 1 bar, it can only hold about 0.3% air by volume.[1]

When water is rapidly heated using a pulsed infrared laser to temperatures well below boiling point, the initial expansion is followed by an apparent contraction and then a re-expansion. The first expansion phase occurs more slowly than the timescale for bulk H-bond re-structuring of the water, as determined from vibrational bands in the Raman spectra. The second phase of the expansion is caused by hydrodynamic effects and is accompanied by morphological changes resulting in light scattering, as well as droplet spallation [70].

As the temperature decreases, an increase in viscosity is observed, which is especially noticeable in supercooled water. The cooperative formation of an open hydrogen-bonded network is observed as temperature decreases. This structure is formed by stronger hydrogen bonding, giving rise to larger clusters and reducing easy traveling (increased viscosity) [165].

The effects of heat treatment on the biological properties of water strongly depend on the object exposed. Fenkes *et al*. have discovered that an upward thermal shift from cold acclimation (8°C) to 13°C reduces salmonid sperm swimming speed, while an increased activation temperature also lowers the proportion of motile cells [71]. The authors consider such effects to be caused by changes in the number of thermosensitive ion channels. Many publications indicate that the soaking of seeds in hot water at 80–90°C with shaking followed by dipping in chilled water results in effective seed decontamination from *Escherichia coli* and *Salmonella* [72, 73].

However, certain pathogens, such as *Legionella pneumophila* and *Mycobacteria avium*, tend to be detected at greater frequencies in hot water systems than in cold water [74]. There is strong evidence of elevated hydrogen metabolism in hot water microbes. Hot waters in electric water heaters can contain as much as three orders of magnitude more H_2 than influent cold water due to metal corrosion [75, 76]. Such elevated H_2 levels enhance the growth of hydrogen oxidizing bacteria and hydrogen metabolism [76]. Moreover, the elevated proportions of hydrogenase genes, as well as chaperon genes for the correct folding and functioning of hydrogenase in *Legionella pneumophila* provided strong evidence of stimulated hydrogen metabolism in hot water.

ELEVATED PRESSURE

In the same way that a high-density crystalline phase is formed, liquid water also undergoes significant structural changes at high pressure. The viscosity, self-diffusion and compressibility of water contribute to achieving approximately 200 MPa pressure. At higher temperatures, these changes are induced at higher pressure values (for example, at 127°C, a pressure of 600 MPa is required, and at 177°C, changes will be achieved at 1 GPa [77].

Viscosity is one of the properties of water, the change of which will have a stronger effect on biological systems. The diffusion velocities of reactants and products strongly depend on the medium viscosity which determines the liquid-phase reaction rate. Water viscosity, which rapidly increases at low temperatures, in contrast to expectations does not increase with growing pressure, as common for other liquids. Water shows anomalous behavior at 30°C and low pressure: while the pressure in this case increases, water's viscosity unexpectedly decreases, not increases [78]. The weakening of hydrogen bonds caused by the reduction in intermolecular distance allows freer displacement of water molecules. The viscosity decrease appears to be minimal at around 150 MPa, increasing thereafter to follow the classical behavior for higher pressures [79].[2] At sufficiently high

[1] Watreco. VPT – Vortex Process Technology. URL: https://www.watreco.com/technology. Accessed August 31, 2021.

[2] Revised Release on the IAPS Formulation 1985 for the Viscosity of Ordinary Water Substance. Erlangen, Germany: The International Association for the Properties of Water and Steam; 1997. 15 p. https://doc.modelica.org/Modelica%204.0.0/Resources/Documentation/Media/Water/IF97documentation/visc.pdf. Accecced May 24, 2023.

pressure (above 200 mPa), water viscosity increases significantly compared to that at the atmospheric pressure. The specific volume and heat capacity of water both decrease monotonously with pressure as a result of the weakened hydrogen bonds that are its energy storage.

The dielectric constant increases with pressure. This, in association with the increase in density, manifests itself as a reduction in the strength of electrostatic interactions [80]. Density increases with pressure [81], while the fundamental tetrahedral H-bonding pattern is preserved at up to about 1 GPa: the stability limit of liquid water at 27°C [82]. A study of the densities of trimethylamine *N*-oxide aqueous solutions measured at pressures of 0.1 to 100 MPa demonstrates that the concentration dependence of densities is minimal at pressures of 75 MPa and higher. The apparent molar volumes of trimethylamine *N*-oxide in aqueous solution increased as the pressure grew, if temperature and concentration were not too high. Considering these thermodynamic criteria, it can be concluded that such hydrophobic substances act as structure-forming agents in water [83].

As an explanation for all these effects, there appears to be an increase in interpenetration of hydrogen bonded networks at about 200 MPa (at 17°C). Interpenetration of hydrogen bonded clusters is preferred over more extreme bending or breaking of the hydrogen bonds. This structural arrangement of liquid water at high pressures corresponds to that detected at neutron scattering [84], suggesting that the structuring of liquid water at high pressure is similar to the structure of ice phases obtained at high pressure [85].

Study of the high-pressure effects on the properties of solutions are essential in understanding the functioning of microorganisms living in the ocean under pressures of up to 100 MPa. Such pressure can affect the structure and density of aqueous solutions of osmolytes that influence the osmotic pressure inside organisms and the stability of their enzymes [81].

BUBBLE GENERATION AND BUBBLING

Micro- and nanobubbles (MNBs) have been a subject of intensive research over the past decade.

Gas particles exist with sizes ranging about several hundreds of nanometers and with number volume density in the range of approximately from 1 to 5 (up to 12) 106 cm^{-3} [86]. The characteristics of MNBs include the increased solubility of gases in liquids, reduced friction, either negative or positive zeta potentials and the generation of free radicals [87–89]. Some authors indicate an abrupt increase in the electrical conductivity of MNB water [90], while others provide evidence of reduced conductivity compared to purified water [91]. It is evident that air bubbles in water cannot be viewed as neutral and that ions are closely involved in the generation mechanism of these bubbles, thus influencing the properties of a solution. Furthermore, the selective adsorption of dissolved anions at nanobubble (NB) interface contributes to their stabilization [86]. The pH value of the solution may be observed to either increase or decrease, which also supports this hypothesis [92]. Electric fields emerging around bubbles due to their polarization affect one another. Based on NMR results, the number of NBs is positively correlated with the relaxation time, T2, of the water. The increase in T2 with the generation of NBs indicates that the mobility of the water molecules increases [93].

In addition, ultra-fine hydrogen-bubbled water has been shown to obtain properties different from those of reductive hydrogen water and tap water. The authors proved that the pH and oxidation-reduction potential were changed by 0.6 and almost 1000 mV, respectively, when compared to tap water [94]. It was also found that, as in the case of shaking, reactive oxygen species (ROS) are produced by NB water. The fluorescent response to ROS was found to be maintained within 2 days, and the number of ROS has a positive correlation with the NB number density in the water [95]. The positive and negative biological effects of NBs depend on the size of the organism and its susceptibility to ROS, NB size and amounts, temperature, flow rate and nature of the liquid. NBs have been reported to produce negative effects on bacteria and positive effects on yeast [96].

Recently, there has been considerable focus on the application of MNB technology in biological processes. Water containing MNBs has been reported to accelerate the growth of plants and shellfish, and has also been used in the aerobic cultivation of yeast [97]. Ebina *et al*. showed that oxygen-NB water promoted the growth of plants, fish, and mice [98]. Kurata *et al.*, who applied oxygen micro-bubbles in an osteoblast cell-culture system, reported greater alkaline phosphatase activity, related to increased osteoblastic cell activity [99]. Park *et al*. found that the fresh weights of micro-bubble treated lettuces were 2.1 times greater than those of the macro-bubble treated lettuces, when grown under the same conditions [100]. Ushikubo *et al*. showed that when barley coleoptile cells were floated in water after the generation of oxygen MNBs, cytoplasmic streaming rates inside the cells were accelerated [101]. Moreover, NBs may provide a transport mechanism for gas delivery to a membrane or cell and thus alter the cell function [102, 103]. Liu *et al*. also demonstrated that the germination rates of barley seeds dipped in water containing MNBs were 15–25% greater than those of the seed dipped in distilled water. Tap water containing NBs reduces bacterial diversities and decreases the deposition of mineral precipitation [104]. The germination rates of seeds dipped in water containing NBs are 15–25% higher and are characterized by greater spin-lattice relaxation times and spin-spin relaxation times measured by the NMR method [93].

VORTEXING, SHAKING, AND INTENSIVE VIBRATION TREATMENT FOLLOWED BY DILUTION STEP

One of the most common mechanical effects on water is vigorous shaking. This technology implies using a vortex mixer, magnetic stirrer and other similar devices, as well as ordinary shaking. It has been shown that the vortex-processed water has a higher electrical conductivity than non-treated water (2.8–2.9 dS/m *vs* 2.5 dS/m), as well as reduced viscosity (by 3–17%, depending on water quality) and increased heat capacity (by 3%).[3] Mechanically treated aqueous solutions also produce biological effects. A study examining the effects of vortex-processed water further used on tomato plants demonstrated that the stem height and width of the plants were significantly greater, regardless of their culture. Both higher electrical conductivity and higher availability of nutrients in the vortex-processed water might have given the tomato plants a slight advantage [105].

Some simple organisms are sensitive to mechanically treated water. Dinoflagellates enhance their bioluminescence in response to a medium (seawater with salts) exposed to shaking. This effect is observed in 10 min after mechanical exposure [106]. RNS60, a physiologic saline solution containing oxygen NBs, generated by subjecting normal saline to Taylor–Couette–Poiseuille (TCP) flow under elevated oxygen pressure, has been shown to inhibit the expression of proinflammatory molecules in glial cells via phosphatidylinositol-3-kinase (PI3K)-mediated upregulation of IκBα. Thus, RNS60 treatment decreases the activation of astrocytes and microglia and reduces neuronal a poptosis in the brain of mice after traumatic brain injury [107]. RNS60 solution also exhibits immunomodulatory effects [108]. Long-lived luminescence in the blue region was found to occur in deionized water saturated with atmospheric gases following mechanical shaking.

Effects of intensive vibration treatment combined with serial dilution steps on the properties of solutions have been studied to a much greater extent. This technology is often used to prepare ultra-dilutions or high dilutions (UHDs) which refer to extremely low molarity (frequently above the number of Avogadro) preparations of biologically active substances [109]. Due to a combination of various physical influences (like pressure, temperature, NB formation, etc.), this technology should, therefore, be considered a complex physical process that changes the properties of water [3, 110–112]. The properties of UHDs prepared using this technology (for example, electrical conductivity, dissolved gas concentration, ultrasonic wave velocity, pH, surface tension, dielectric constant, and spectral response) are quite different from those of the initial substance solution and the solvent (water), and can be explained by the formation of nanoassociates [111–119]. Another example of anomalous properties of such an UHD is the fact that oxygen molecules in aqueous solutions subjected to external physical action transition from the triplet to the singlet state. This may indicate the possibility of overcoming or bypassing the quantum exclusion principle [3, 120]. Furthermore, for dilutions saturated with NBs generated by turbulent flow mixing, it has been shown that the H_2O_2 concentration in the solution increases with each successive dilution step. This suggests that the generation of free radicals may also alter the concentration of hydrogen peroxide obtained from water molecules, while atmospheric oxygen increases in the process of vigorous shaking [4]. The ROS generation rate has been found to increase exponentially with an increase in the frequency of mechanical action. The major pathways for hydrogen peroxide generation are probably associated with the formation of singlet oxygen and its further reduction. The alternative pathway is the formation of hydrogen peroxide as a result of hydroxyl radical recombination [121]. The pH of water tends to increase immediately after mechanical exposure. The droplet evaporation method shows that succussion of pharmaceutical preparations obtained as described (compared to gently mixed samples) induces the formation of structures characterized by a greater disorder (parameter entropy), increased gaps between the structure elements (parameter lacunarity), and smaller complexity (parameter local connected fractal dimension) [122]. According

[3] Watreco. VPT – Vortex Process Technology. URL: https://www.watreco.com/technology. Accessed August 31, 2021.

to the literature, the addition of substances in ultra-low concentrations leads to a change in the structure of water, i.e., to a change in its hydrogen bonds [123–125]. It has been demonstrated that near-ultraviolet scattering spectra of water change significantly following intensive vibration treatment combined with serial dilution step, with the changes persisting for several hours after exposure [126]. Subsonic-frequency mechanical oscillations have been shown to increase the redox potential of water, which is also maintained for a considerable period of time [127].

There is also data to indicate that molecules of the original substance are preserved in UHDs [4, 118, 128, 129], while common vigorous shaking (using a vortex mixer or similar devices) removes bubbles from the solution, including those with adsorbed impurities. Multiple serial dilutions preserve the molecules of the initial substance. These may become nucleation sites for forming stable [130–133] NB structures generated during the vigorous mechanical process (like preparation of UHDs) and highly-organized water around them [134]. The possibility of the presence of initial substance molecules, even in the high dilutions, can also be explained by the froth flotation. This does not mean, however, that these residual molecules are responsible for the high dilution unique properties [2, 4, 10, 118, 129, 135, 136]. The spontaneously formed nanoassociates may represent the carrier of activity that determines the special physical, chemical, and biological properties of UHDs [113, 119].

Long-lived nano and micro entities of an unknown nature are also detected experimentally in UHD substances [118, 134, 137–139]. The stability of these clusters may be achieved via the presence of deuterium [123, 140] in water, residual amounts of the initial substance [118, 129], or impurities (ions, silicates) released from the surfaces of the containers used for serial dilutions combined with intensive vibration treatment [141]. It has been shown experimentally that nanosilica can self-assemble into trimeric structures [142–147]. Adsorption of ions (from glass or water) or hydrophobic molecules on the surface of heterophase elements makes them more stable. The longevity of NBs and its correlation with the material of the bottle may be associated with the negative charge of the NBs. The glass surface becomes negatively charged due to silica hydrolysis and SiOH dissociation into SiO^- and H^+. Therefore, the charged NBs support the stabilizing electrical interaction [148, 149].

Individual density inhomogeneities are believed to be organized into giant heterostructures, the topology of which depends on the primer, i.e., the residual initial substance [140]. These nanostructures can be maintained through the dilution process due to their drive for hydrophobic surfaces (a plastic pipette tip) or electrostatic interactions, in a case with a glass pipette/glass chip or a glass container surrounded by an electric field, forming new clusters in each dilution [150].

It may be concluded that a serial dilution process combined with intensive vibration treatment is a good technique for producing stabilized water structures in water solutions. The special biological properties of aqueous solutions exposed to the serial dilution process combined with intensive vibration treatment are also determined by the specificity of the initial substance. They offer new opportunities for treating various diseases, as has been demonstrated in a number of studies [151–159]. This also can be useful in the technology where the treatment of piezoelectric ceramics by the corresponding UHDs during the hot pressing caused changes to the physical features of the resultant ceramic samples [160]. Thus, in spite of high-temperature processing, the activity of UHDs is retained. Serial dilutions of a solvent containing no initial substance (control) followed by intensive vibration treatment also result in the formation of nanostructures different from those in water. However, their properties (activity) will lack specificity [161].

Agricultural studies have demonstrated that adding extremely diluted substances results in increased chlorophyll production, significantly changes the amino acid profile and amino acid production as well as photosynthesis, germination rates and metabolism. The ability of highly diluted formaldehyde to affect the rate of demethylation/re-methylation of veratric acid by the *Rhodococcus erythropolis* bacteria was shown using electrophoretic and microscopic techniques [162]. Also, the germination rates of wheat seeds treated with UHDs increase significantly when the number of strokes is increased during the dilution process [163, 164]. All of these (and many other) physicochemical reactions, as well as effects on living systems exposed to the water and aqueous solutions obtained during the intensive vibration treatment and dilution process, stress the importance of this approach in many disciplines.

CONCLUSIONS

This review shows that physical treatment of water can induce changes both in physicochemical and biological properties of water and aqueous solutions. Many of the properties listed in the table may change in response to certain exposure.

As the structure of water is responsible for its properties, most types of exposure are directed at the clustering of water molecules (formation, destruction, and association), changing intermolecular distance and the nature of hydrogen bonding, as well as the formation and collapsing of bubbles.

These structural modifications may change the main properties of water, such as: heat capacity; molar volume; thermal expansion coefficient; isothermal compressibility coefficient; air solubility in water; water expansion with increasing temperature; and viscosity with decreasing temperature. It has been experimentally demonstrated that heating makes water less compressible and decreases air solubility in water, and cooling enhances its viscosity, while changes in the molar volume and expansion rate have a non-monotonic nature.

Acoustic exposure also results in significant changes. This type of exposure makes the structure of water coarse-grained, i.e., it increases the number of large clusters, increases pH and temperature inside a cavitation bubble and leads to the formation of various free radicals.

High pressure enhances the physical properties of water such as viscosity, self-diffusion, and compressibility. Water viscosity increases considerably at quite high pressure. However, water shows anomalous behavior at 30°C. Water viscosity decreases with increasing pressure and can drop to 150 MPa, increasing thereafter to follow the classical behavior. It has also been shown that the specific volume and heat capacity of water both decrease monotonously with increasing pressure, while dielectric constant and density tend to increase.

Some researchers indicate an abrupt increase in the electrical conductivity of micro-nano bubbled water, whereas others report reduced conductivity when compared to purified water. It has been proved that the pH and oxidation-reduction potential are changed by 0.6 and 1000 mV, respectively, when compared to the initial water. For NB processed water, there are changes in the spin-spin and spin-lattice relaxation times, ROS are formed as well as the increased solubility of gases in liquids and reduced friction are observed.

Vortex process technology results in the increased electrical conductivity of water and reduced viscosity as undissolved gases are removed. However, there is an increase by 3% in electrical conductivity after vortex process technology treatment. Intensive vibration treatment and dilution processes also exert pronounced effects on water. When treated by this method, water can change some of its characteristics, such as: electrical conductivity; dissolved gas concentration; ultrasonic wave velocity; pH, surface tension; dielectric constant; and spectral response. The vigorous mixing of the solution results in the increased generation rate of ROS with an increase in the frequency of mechanical action, increased pH, altered near-ultraviolet scattering spectra of the water, as well as enhanced oxidation-reduction potential. Nanoassociates formation is one of the possible explanations of this phenomena.

With regard to the effects on living systems, treatment of water using various methods, such as ultrasonic exposure, bubble generation, intensive vibration treatment, or vigorous mixing, including that with serial dilution process, changes the biological properties of water. Many authors report improvement in the growth and development of organisms and plants soaked in the processed water. Water exposed to various types of mechanical stress produces positive effects on the germination rates of seeds, plant weight and stem width, and the growth of fish and mice. From the practical point of view one of the most important abilities of mechanically-treated dilutions is the ability to exert influence on the initial substance. This is useful for improving the material features, and for medicines with the physical mechanism of action affecting the target molecules. Most data on the biological effects of processed aqueous solutions were experimentally obtained for solutions exposed to mixing combined with serial dilution steps. Other test factors have been barely studied, so further investigations are required to develop this topic.

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Authors' contributions

E.S. Don – conceptualization, data search, writing the original draft;

G.O. Stepanov – conceptualization, review and editing the text of the manuscript;

S.A. Tarasov – supervision, review and editing the text of the manuscript.

Conflicts of interest

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: E.S. Don, G.O. Stepanov, and S.A. Tarasov are employees of *Materia Medica Holding* (fully or partly). Employees of *Materia Medica Holding* made a decision to publish the work and took part in the manuscript writing. *Materia Medica Holding* produces the drugs based on the technology of serial dilution process combined with external treatment.

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