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Differences in the Properties of Drinking Water and Cellular Water in Various Organs Can be Confirmed by Measuring Aquaporin Permeability

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Aquaporin; Water permeability; Mineral water; Cell water; ATP

1. Abstract

This paper investigates the water permeability of several aquaporins (AQPs) and elucidates water scientifically. AQP is a membrane protein with a hole which water pass through. There are 13 kinds of AQP in humans. Mineral water could be classified by examining six types of AQP. Furthermore, it was found that the water in the cells of the organ was also water with different AQP permeability for each organ. There was a certain degree of correlation between AQP distributed specifically in organs and AQP permeability of water in organ cells. In other words, it became clear that there is water that accumulates specifically in organs. Furthermore, it was found by measuring the amount of ATP in organs that the activity of the cells of the organ increased when AQP highly permeable water was drunk.

2. Introduction

No one has any objection that water is indispensable to living organisms. In addition, some people believe that water is not just a solvent but a special function. However, most of the reports demonstrating that effect is scientifically unreliable. If mineral water really has the power to promote our health, it is worth scientifically proving. In this report, the permeability of water to six types of human AQPs was investigated, and water was scientifically elucidated. AQP is a membrane protein with a hole which water pass through Dr Peter Agri [1] discovered and was awarded the Nobel Prize in chemistry in 2002 for this discovery. Many researchers [2-4. have studied the distribution, structure, and expression of human aquaporins in tissues. The studies by King and Agre [5] helped elucidate the relationship between human health and aquaporin expression. On the other hand, the reason why there are 13 types of aquaporins in humans has not been clarified Sakurai et al [6]. Reported thirty-six types of aquaporins are known in plant rice, and special functions in each tissue are discussed but not clear. Kitagawa [7-8] has found that the water permeability of human aquaporins depends on the type of water. For example, the water permeability of aquaporin 1 is clearly different between tap water and natural mineral water. Similarly, the water permeability of other aquaporins depends on the type of water. It was thought that this could be used as a means to investigate the properties of water, and the permeability of aquaporins in various waters was investigated. This idea can be used to examine water in the cells of mouse organs. This report reports that the water in the cells of organs such as the brain, kidney, liver, lung et. al. is also different. Furthermore, it was found by measuring the amount of ATP in organs that the activity of the cells of the organ increased when AQP highly permeable water was drunk.

3. Materials and Methods

3.1. Tap Water and Natural Mineral Water

Tap water for the cities of Sapporo, Sendai, Tokyo, Nagoya, Osaka and Fukuoka was distributed by each prefecture's waterworks bureau. As representatives of AQP1, AQP2, AQP3, AQP4, AQP5 and AQP7 high permeability water, the water in Oita-Hita prefecture (Hita Tenryosui), in Toyama prefecture (Kurobe natural water), in Kagawa prefecture (Mt. Shippo water), in Aichi prefecture (Athlete water), in Oita-Kusu prefecture (Kusu natural

water) and in Kagoshima Prefecture (Hot Spring water 99) was used. Many commercially available waters from Japan and around the world were used in this test. These waters were used for aquaporin permeability experiments without osmotic adjustment. As a control, RO membrane treated water from which solutes were removed as much as possible was used. Commercially available RO membrane water (Sanei, Kumamoto, Japan) was also used.

3.2. Rocks, Ceramics and Homeopathic Remedies Treatment

Rock, ceramic and homeopathic remedies were used to alter the aquaporin permeability of water. The rocks used were feldspar (Kiyoseki, Gunma feldspar limited partnership company, Gunma, Japan), hornfels (Tenkouseki, Only Co., Ltd., Miyazaki, Japan), and ceramics made from fired iron and clay (Cosmic, Cosmic LLC, Hiroshima, Japan). These rocks and ceramics were added to RO membrane water in an amount of 10% by weight, and the water was allowed to stand at room temperature for 24 hours. Homeopathic remedies can also be used to change water permeability. Aconite napellus (Anx), Sabal Serrulata (Ssx), Euphrasia officimalis (Eox) and China medicated potency (Chx) were obtained from Ainsworths Homeopathic Pharmacy, Alternative Medicine (London, UK). The stock solutions of these remedies (mostly water) were further diluted 100 times with RO membrane water, and the water left at room temperature for 24 hours was used.

3.3. Collection of Cell Water from Mouse Organs

Fifteen-week-old female DDY mice were purchased from Japan SLC, Inc. (Shizuoka, Japan). Blood was collected from mice kept for 5 and 10 weeks while drinking tap water and mineral water (Hita Tenryosui). On the other hand, other mice were kept drinking tap water for 5 weeks, anesthetized with chloroform, and blood was collected from the heart using a syringe. The brain, lungs, heart, liver, kidneys, intestines, adipose tissue, and skin tissue were then removed using a scalpel. The hair was cut from the skin tissue and the attached fatty tissue was removed to obtain skin. The lungs, heart, liver, and kidneys were injected with saline through blood vessels to wash away blood, and the organs were chopped with scissors and washed with saline. The brain, intestine, adipose tissue, and skin were minced and washed with saline. Freeze-drying was performed to obtain organ cell water. Each organ was set in a freeze dryer (Labconco freeze drying FZ-12, USA), and after drying, the water collected as ice in the cold trap was melted with a dryer and collected as cell water.

3.4. The amount of ATP in Each Dried Organ was Measured.

The amount of ATP in each freeze-dried organ was measured. The dry solid matter of each organ was ground in a mortar, a certain amount was weighed, and RO membrane water was added to make a 10% suspension. After stirring thoroughly, the mixture was centrifuged at 1,000 rpm for 5 minutes, and the supernatant was diluted to approximately 1,000 with RO membrane water and used for measurement. ATP Detection Assay Kit – Lumines (Cayman Chemical Company, Michigan, USA) was used to measure ATP, and a small tabletop luminometer (Gene Light GL-220, Osamu Ikeda Co., Ltd., Tokyo, Japan) was used to measure fluorescence.

3.5. In Vitro Transcription of Aquaporin Genes, Microinjection of Xenopus Oocytes and Measurement of Water Permeability

The human aquaporin genes (AQP1, AQP2, AQP3, AQP4, AQP5 and AQP7) inserted in the pXβG-ev1 vector were furnished by Dr. Ishibashi, K., Dr. Yasui, M., and Dr. Sasaki, S. The capped complementary RNA (cRNA) was synthesized using T3 RNA polymerase of the mMESSAG mMACHINE High Yield Capped RNA Transcription Kit (Cat no.: AM1348, Ambion, USA) after linearization of the aquaporin pXβG-ev1 constructs as described by Kitagawa et al [7]. The synthesized RNA samples were purified, and the concentrations were measured. Oocytes (1.0– 1.2 mm in diameter) of stage V–VI were incubated in 0.3mg/ml collagenase (*Clostridium histolytium*, Fujifilm-Wako, Oosaka, Japan) and 1mg/ml bovine serum albumin (Fujifilm-Wako, Oosaka, Japan) solution [100 mM NaCl, 2 mM KCl, 1 mM $MgCl_2$, and 5 mM Hepes-Tris (pH 7.5)] at 20 °C for 2.5 h. The exfoliated oocytes were washed with Modified Barth's Saline (MBS) medium [88 mM NaCl, 1 mM KCl, 2.4 mM $NaHCO_3$, 0.4 mM Ca $(NO_3)_2$, 0.4 mM $CaCl_2$, 0.8 mM $MgSO_4$, 100mg/L Na-penicillin, and 100mg/L Streptomycin, 15 mM Tris-HCl (pH 7.4)]. The 25 nl of cRNA (2.5~10 ng) or 25nl water was injected into oocytes using a Nanoject injector (Narishige, Tokyo, Japan). The injected oocytes were cultured in MBS (200 $mOsm_{in}$) prepared by RO membrane permeate water for 48 h at 20 °C. For determination of water permeability, the injected and cultured oocytes were transferred into water (0 $mOsm_{out}$), and the oocyte swelling velocity was measured with a digital camera and calculated with Motic Images Plus 21S software (Shimazu, Kyoto, Japan). Osmotic water permeability (Pf) was determined from the initial slope of the time course of V/V_0 ($d(V/V_0)$ /dt), initial oocyte volume (V_0=9 x 10-^{4} cm^3), initial oocyte surface area (S=0.045 cm^2), and molar volume of water (Vw =18 cm^3 mol-^{1}): $Pf=V_0[d(V/V_0)dt] / [S \times Vw(Osm_{in}-Osm_{out})]$.

4. Results

4.1. AQP Pf of tap or Mineral Water

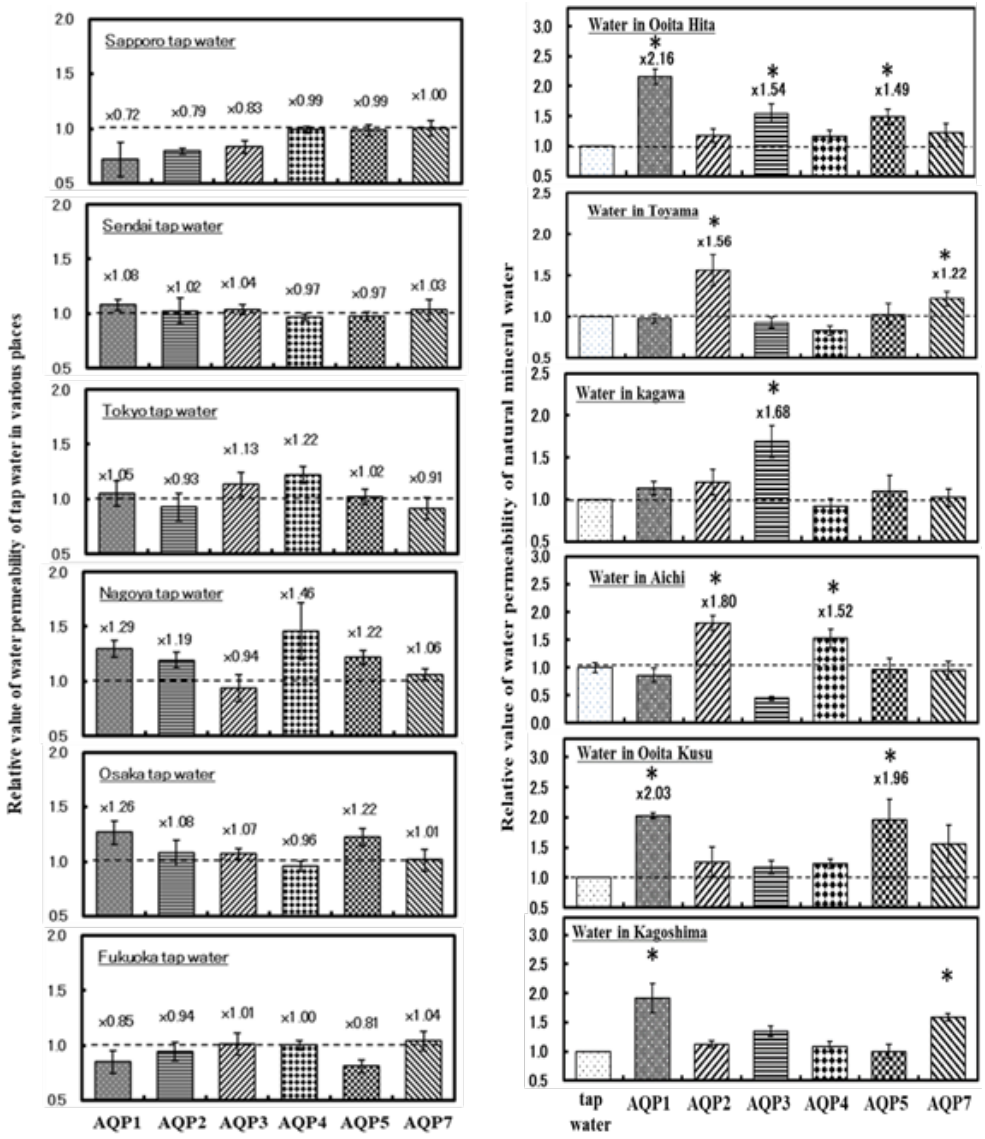
There is a certain value for water permeability for each AQP. However, we found that the value varies with the type of water. In other words, the difference in the type of water is indicated by the difference in water permeability to AQP. It was the first time in the history of water research that it was possible to show the difference in the properties of water with such clear numerical values. To investigate the AQP permeability of water, *Xenopus* oocytes are used. One type of human AQP gene cRNA is injected into the oocyte. Human aquaporin protein is expressed on the cell membrane upon incubation for 1 to 2 days. When this oocyte is put in various kinds of water and the expansion coefficient is measured, different water permeability values for the same AQP are obtained

by the type of water. When AQP permeability of various mineral water was examined by this method, it was clearly confirmed that the permeability differs depending on water. However, in order to compare the difference in permeability depending on the type of mineral water, water as a reference is necessary. It would be easy to accept if AQP permeability of tap water is used as a basis for comparison. Therefore, the AQP permeability of tap water in each city was examined. First of all, it is to calculate the average value of water permeability for AQP 1 of tap water in each place. Similarly, average values for other AQPs are calculated. Based on the average value, the results of aquaporin permeability of tap water in each city of Japan are shown in Figure 1a. As the results, the tap water in Sendai City showed the most average value for AQP 1 to 7. The aquaporin permeability of the natural mineral water was compared with that of Sendai City's tap water. It was recognized that the permeability of natural mineral water to AQP was higher than that of tap water in general. And there was also mineral water with high water permeability for certain AQP. Figure 1b shows typical AQP permeability patterns of water with high permeability to each AQP. The water of Oita-Hita prefecture (Hita) with high permeability to AQP 1, the water of Toyama prefecture with high permeability to AQP 2, the water of Kagawa prefecture with high permeability to AQP 3, the water of Aichi prefecture with high permeability to AQP 1 & 4, the water of Oita-Kusu prefecture (Kusu) with high permeability to AQP 1 & 5, the water of Kagoshima prefecture with high permeability to AQP 1 & 7 are shown in the Figure 1b. Hita Tenryosui in Oita Prefecture (Hita) water has particularly high permeability to AQP1. Water with this aquaporin permeability pattern is often found in waters sold in bulk. Kurobe natural water in Toyama Prefecture has particularly high permeability to AQP2. Water with this aquaporin permeability pattern is very rare. Water from Mt. Shippo in Kagawa Prefecture had significantly high permeability to AQP3. The water from the spring in Lourdes, France, which is well known as miracle water, and the Zero magnetic field water, which is known as a power spot in Nagano Prefecture, are also characterized by their high permeability to AQP3. It is very difficult to explain the benefits of water. The similarities in aquaporin permeability patterns may suggest common properties of water. None of the waters examined so far had particularly high permeability for AQP4. Athlete water in Aichi Prefecture had high permeability to AQP 2 & 4, but waters with high permeability to AQP 1 & 4, such as Canadian Crystal Geyser water, are often found. Kusu natural water in Oita Prefecture has particularly high permeability to AQP5, but also particularly high permeability to AQP1. Water with particularly high permeability to AQP5 often exhibits a pattern of high permeability to AQP1 and other AQPs. Hot spring water 99 from Kagoshima Prefecture has particularly high permeability to AQP7, but also particularly high permeability to AQP1. No water was found that had high AQP7 permeability alone. Also, there are very few waters that show AQP permeability patterns similar to hot spring water 99.

4.2. AQP Pf of Artificially Altered Water

Aquaporin highly permeable water can be made by putting rocks and ceramics in tap water and leaving it overnight. An example is shown in Figure 2a, Feldspar (Kiyouseki) obtained from a mine in Katashina Village, Gunma Prefecture, is said to have various health benefits. When this feldspar was put in tap water and left overnight, it changed to AQP1 highly permeable water. Similarly, hornfels (Tenkouseki) produced in Takachiho, Miyazaki Prefecture, are said to have various health benefits. When this stone was added to tap water, it changed to AQP 1, 5 & 7 highly permeable water. Furthermore, when ceramics (Cosumic) obtained by firing clay and iron sand were put into tap water, the tap water changed to AQP 1 & 5 highly permeable water. The transformation of water containing these rocks and ceramics into AQP highly permeable water will help explain the health benefits of these waters. It is presumed that natural mineral water was also transformed into AQP highly permeable water by touching underground rocks. The conversion of tap water into AQP highly permeable water occurs not only by dissolving rocks and ceramics, but also by dissolving certain substances. However, in this case, it is common sense to think that the dissolved substance acted on the aquaporin molecules. The homeopathic effect is most appropriate to demonstrate that the dissolved material has caused a change in water. Homeopathic medicine, which is widely accepted in Europe, is a remedy-based treatment for illness. Remedy is infinitely diluted water containing substances that induce the same symptoms as the symptoms of the disease. This water-based treatment is called homologous therapy. The results are shown in Figure 2b. Aconite napellus (Anx) increased the AQP1&2 permeability of tap water by 1.26-1.3 times, Sabal Serrulata (Ssx) increased AQP1,2,4 & 5 permeability of tap water by 1.35 to 1.72 times, and Euphrasia officimalis (Eox) increased AQP1,2 & 4 permeability of tap water by 1.23 to 1.53 times higher, and China medicated potency (Chx) increased AQP2,3,4,5 & 7 permeability of tap water by 1.20 to 1.67 times higher. The remedy clearly had the effect of altering the properties of water. The homeopathic world claims that remedies change the structure of water, and that water remembers that structure.

Figure 1: Aquaporin Permeability Frequency (AQP Pf) of tap and Natural Mineral Water.

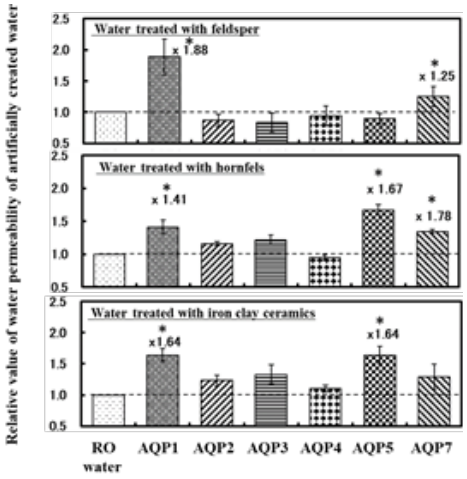


(a) AQP Pf of tap water in various city

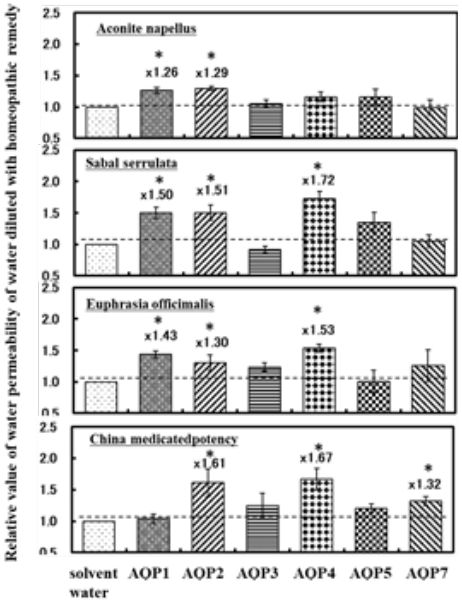
(b) AQP Pf of natural mineral water

Figure 1: Relative value of aquaporin permeability frequency (AQP Pf) of tap water in each city and natural water in various places. (a) AQP Pf of tap water in Sapporo, Sendai, Tokyo, Nagoya, Osaka, and Fukuoka, (b) AQP Pf of natural water in Oita Hita (Hita Tenryosui), Toyama (Kurobe Sui), Kagawa (Shipposan sui), Aichi (Athlete Sui), Oita Kusu (Silicon Megumi), Kagoshima (Hot Spring Water 99). The water permeability of the oocytes. injected with the cRNA of the indicated aquaporins were determined in each city and natural water in various places (10–15 eggs were injected and measured for each aquaporin in each water samples (* : $p < 0.05$).

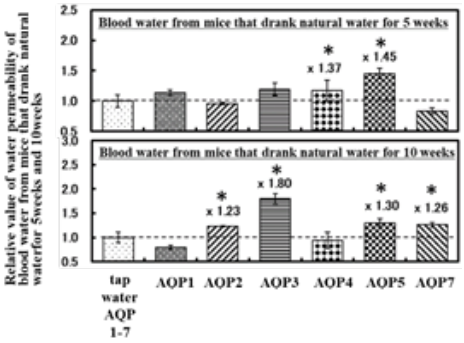
Figure 2: Relative value of aquaporin permeability frequency (AQP Pf) of water treated with rock ceramic and homeopathy remedy, and AQP Pf of blood water in mice fed with high aquaporin permeable water.



(a) AQP Pf of water treated with rock and ceramic.



(b) AQP Pf of water treated with homeopathy remedy



(c) AQP Pf of blood water in mice fed with high aquaporin permeable water

Figure 2: Relative value of aquaporin permeability frequency (AQP Pf) of water treated with rock, ceramic and homeopathy remedy, and AQP Pf of blood water in mice fed with high aquaporin permeable water. (a) AQP Pf of water treated with rock and ceramic, (b) AQP Pf of homeopathy remedy, (c) AQP Pf of blood water in mice fed with high aquaporin permeable water. Feldspar (Kiyoseki), hornfels (Tenkouseki), and iron and clay ceramics (Cosumic) were added to RO membrane treated water in Oita Kusu at a ratio of 10% by weight, and then allowed to stand for 24 hours. The water permeability of the oocytes injected with the cRNA of the indicated aquaporins were determined in the rock-treated waters (Figure 2a,10–15 eggs were injected and measured for each aquaporin in each water samples. *: $p < 0.05$). Aconite napellus, Sabal Serrulata, Euphrasia officimalis and China medicated potency were added to RO membrane treated water in Oita Kusu at a ratio of 1% by weight, and then allowed to stand for 24 hours. The water permeability of the oocytes injected with the cRNA of the indicated aquaporins were determined in homeopathy remedy treated waters (Fig.2b, 10–15 eggs were injected and measured for each aquaporin in each water samples. * : $p < 0.05$). Twenty mice (DDY, 12 weeks old) were divided into two groups, and one group was given tap water and the other group was given natural water from Oita Hita. Blood was collected from the heart using a syringe at 5 and 10 weeks after drinking water. After the blood was frozen, it was placed in a freeze dryer, and the evaporated water was collected as ice in a cold trap. Aquaporin permeability of plasma water was measured using oocytes injected with aquaporin cRNA (Fig.2c,10–15 eggs were injected and measured for each aquaporin in each water sample. *: $p < 0.05$).

4.3. AQP Pf of water Treated with RO Membrane and Freeze Dryer

The original natural water in Oita Kusu was filtered through an RO membrane to create water without salts. In addition, Oita Kusu natural water was placed in a freeze dryer, and the evaporated water was collected as ice in a cold trap. The water permeability of the oocytes injected with the cRNA of the aquaporins were determined in the original natural water, the RO membrane treated water, and the evaporated waters. The AQP permeability of the mineral water is independent of the minerals and substances contained in those waters (Graph of results omitted). Kusu natural water is characterized by its high permeability of AQP1 and AQP5 compared to tap water (see Fig.1b). Both the RO membrane-treated water and the freeze-dried water showed almost the same aquaporin permeability as the original water (10–15 eggs were injected and measured, $p < 0.05$). Therefore, it is clear that the aquaporin permeability characteristic of mineral water is not the effect of substances such as minerals that are dissolved in water.

4.4. AQP Pf of Mouse Blood Plasma Water after Drinking of AQP High Permeable Water

It can be easily inferred that blood water is closely related to drinking water. In fact, the AQP permeability pattern of plasma water in mice clearly changed when they were fed water with high AQP permeability. When mice were allowed to drink the water in Oita Hita for 5 weeks, the permeability of AQP1, 3, 4, & 5 was higher in the plasma water of mice compared to the plasma water of mice that were allowed to drink tap water (Figure 2c). The pattern of blood-water aquaporin permeability observed at 5 weeks changed at 10 weeks. At 5 weeks, the permeability of AQP4 and 5 was high, but at 10 weeks, the permeability of AQP4 decreased and the permeability of AQP3 and 7 increased instead (Figure 2c). It observed that the pattern of aquaporin permeability in the blood changed over time, even if the mice continued to drink the same water.

4.5. AQP Pf of Water in Cells of Moue Organs

It was demonstrated that the properties of water can be displayed

as patterns of AQP permeability. Using this method, we can also reveal the properties of water in the cells of organs. Since organs obtain water from the blood, it is thought that the properties of water in each organ are the same. However, it has become clear that the properties of water within the cells of organs differ from organ to organ. First, 20 mice were raised with tap water, and blood was collected from their hearts using a syringe. Next, each mouse organ was removed and processed in a freeze dryer to collect the water inside the organ's cells. The freeze dryer has a cold trap that collects the sublimated water. The water collected in this trap is the water that was inside the cells of the organ. The brain, lungs, heart, liver, kidneys, intestines, skin, adipose tissue, and blood were freeze-dried, and cell water from each organ was collected Figure 6. Shows the results of examining the AQP permeability of these waters. The permeability of AQP1-7 was measured for each cell water of nine different organ and tissue. Interestingly, each AQP Pf value of plasma water was close to the average value of each AQP Pf of all organs. Then, when the permeability of blood water to each AQP 1 to 7 is set to 1, the relative value of the AQP permeability of each organ cell water is plotted as a graph. In brain cell water, the Pf values for AQP1, 2, 3, and 7 were lower than the average values for blood water. The Pf values for AQP4 and 5 were high, but among them, the Pf value for AQP4 was the highest, which was 1.22 times higher than AQP Pf values for blood water. In lung cell water, the Pf values for AQP4 and 5 were 1.12 and 1.18 times higher than AQP Pf values for blood water, respectively. In cardiac cell water, AQP2 and 5 Pf values were 1.12 and 1.21 times higher than AQP Pf values for blood water. In liver cell water, AQP1 and AQP2 Pf values were 1.12 and 1.16 times higher than AQP Pf values for blood water, respectively. In kidney cell water, AQP2,3,4, and 5 Pf values were 1.15 to 1.31 times higher than AQP Pf values for blood water, and in particular, AQP3 Pf value was the highest at 1.31 than AQP Pf values for blood water. In intestinal cell water, AQP2, 4, and 5 Pf values were 1.17, 1.27, and 1.25 times higher than AQP Pf values for blood water, respectively. In the cell water of adipose tissue, AQP 7 Pf values were 1.21 times higher than AQP Pf values for blood water. In the cell water of skin tissue, AQP4 and 5 Pf values were 1.43 and 1.26 times higher than AQP Pf values for blood water, respectively. AQP4 is widely distributed in brain tissue, as described by Nagelhus and Ottersen [9], and brain cell water also has a high AQP4 Pf value. AQP1 and 5 are abundantly distributed in lung tissue, as described by Verkman and Matthay [10], and lung cell water has a high AQP5 Pf value. Although AQP1, 3, 4, and 7 are abundantly distributed in heart tissue, as described by Verker [11], heart cell water has a high AQP2 and 5 Pf value. AQP1 and 3 are widely distributed in liver tissue, as described by Gregoire et al. [12], and liver cell water also has a high AQP1 and 2 Pf value. AQP1,2,3,4, and 7 is widely distributed in kidney tissue, as described by Matsuzaki et al. [13], and kidney cell water also has high AQP2, 3, 4, and 5 Pf values. AQP7 is widely distributed in adipose tissue, as described by Lebeck [14], and the cell water of adipose tissue also has a high AQP7 Pf value. AQP1,3 in skin tissue was reported by Bollag et al. [15], but skin tissue cell water has a high AQP4, and 5 Pf value. It is very interesting that the cellular water of organs that derive their water from plasma water is very different from plasma water.

Figure 3: Aquaporin permeability frequency (AQP Pf) of cell water in mouse organ.

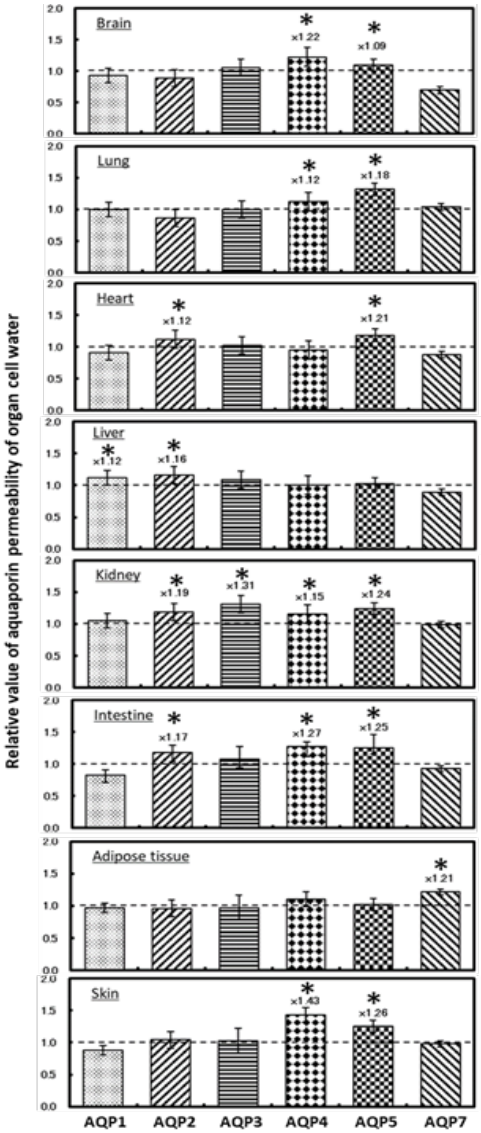


Figure 3: Aquaporin permeability frequency (AQP Pf) of cell water in mouse organ. Brain, lung, heart, liver, kidney, intestine (small intestine + large intestine), adipose tissue, skin tissue and blood were isolated from 20 mice (DDY, 15 weeks old) that were fed tap water. Evaporated water was collected from each sample using a freeze dryer. Aquaporin permeability of each water was measured using oocytes (20-50 eggs, repeat the experiment 3 to 5 times) injected with cRNA (5-20ng) of each AQP 1-7. Aquaporin permeability of water collected from each organ and tissue was expressed as a relative value when the permeability of each AQP 1-7 of water collected from blood was set to 1 (*: $p < 0.05$).

4.6. Amount of ATP in Organs after Drinking of AQP High Permeable Water for 5,10 and 24 Weeks

To confirm whether drinking AQP-highly permeable water activates organ cells, changes in ATP levels were examined. Organs were removed from mice that had been drinking tap water or AQP highly permeable water in Oita Hita after 5, 10, and 24 weeks. Ten of the removed organs were freeze-dried and ground into powder in a mortar, and a certain amount was weighed to measure the ATP content. As shown in Fig.4, the amount of ATP in each organ of mice drinking AQP1 highly permeable water increased compared to mice drinking tap water. It reached its peak at the 10th week and reached the same level as tap water at the 24th week.

Figure 4: Amount of ATP of Cell Water in Mouse Organ.

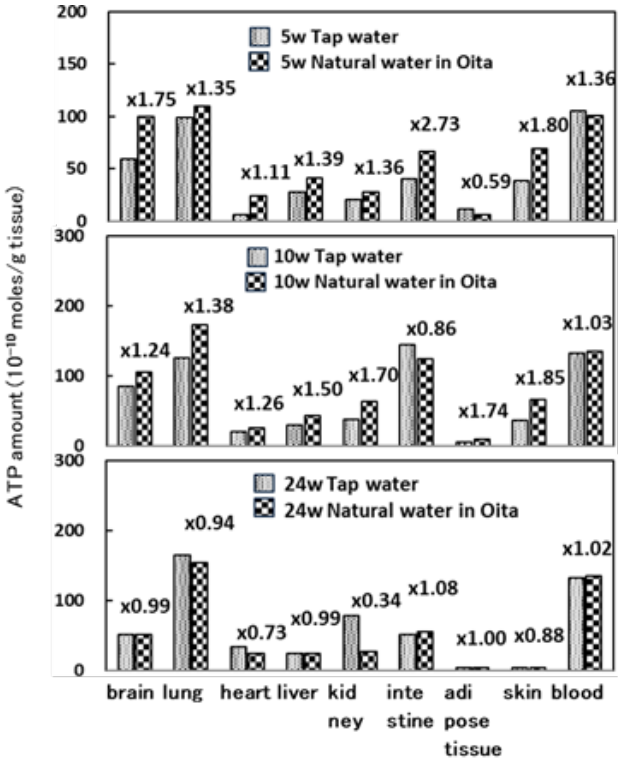


Figure 4: Amount of ATP of cell water in mouse organ. The ATP levels in each organ taken from mice that drank tap water and Oita Hita AQP highly permeable water are shown. The upper, middle and lower figures show the ATP levels in the organs of mice after drinking water for 5, 10 and 24 weeks. The numbers in the figures show the ATP levels in the organs of mice that drank Oita Hita natural water compared to the ATP levels in the organs of mice that drank tap water, expressed as a multiple.

5. Discussion

Aquaporins are channels that exclusively allow water to pass through. Naturally, there is interest in the physiological role of aquaporins, and much research, which are summarized by King and Agre [5], has been conducted at the gene expression level. It was thought that by elucidating the properties of the water that aquaporins pass through, it would be possible to investigate the physiological role of aquaporins. The idea came from observing that the Pf value of aquaporin varies considerably depending on the distilled water used. In fact, there were considerable differences between the cities where tap water was produced. For example, when the average AQP1 permeability value of tap water in cities across Japan is set to 1, the relative value for Sapporo city tap water is 0.72, while that for Osaka city is 1.26. There were also significant differences in the Pf values of natural mineral waters as stated in a previously published paper reported by Kitagawa et al. [7]. As a result of investigating mineral waters in Japan and around the world, the characteristics of Pf values were divided into six patterns. They are permeable water with relatively high AQP1, AQP2 and AQP3 and three types of permeable water with relatively high Pf values of AQP1&4, AQP1&5 and AQP1&7. This indicates that the properties of water can be expressed as a pattern of aquaporin permeability. If water can be expressed in this way, it may be possible to express it in connection with the mysterious phenomena that water exhibits. For example, the water of Lourdes, famous for its miracle water, has particularly high AQP3 permeability. The water at Zero Magnetic Field (Nagano Prefecture), which is famous as a power spot in Japan, also has high AQP3 permeability (Figure 1b). Shipposan water in Mitoyo City, Kagawa Prefecture also has high AQP3 permeability. It will be helpful to find out what kind of effects this water has. The difference in Pf value of AQP does not depend on the minerals or solutes contained in the water. Since there is almost no change in Pf value even if water is treated with an RO membrane or freeze-drying, the difference in Pf value is due to the difference in the water itself, excluding minerals and solutes. What determines the Pf value of water itself. One answer may be the action of rocks, etc. that come in contact with water. The patterns of Pf values of water treated with feldspa, honefels and iron clay ceramics are slightly different even if the same water is used. In this case, analysis showed no evidence that minerals had leached from the rock. What is interesting is that the pattern of Pf values changes when adding homeopathic remedies, which are mostly water. It was confirmed that the Pf value of water changes without adding minerals or solutes to the water. On the other hand, when a solute is added to water, the pattern of Pf values clearly changes. Although data were not shown, the pattern of Pf values changes when silicon, natural salts, certain fermentation products, and cosmetics are added to water. What is interesting is that aquaporin permeability is apparently altered by certain types of electric current treatment or electrical treatment of the hexagonal bolt. The hexagonal bolt is called vG7 and is said to produce special water (quantum water) reported by Tadano et al. [16]. Also, although data was not shown, the pattern of Pf values did not change with heating, microwave treatment, and ultrasonic treatment. The maintenance period of the water Pf value pattern will vary depending on the container in which it is maintained. At least, the pattern of Pf values for bottled water did not change after one year. One of the results of this paper was to demonstrate that the properties of water itself

can be distinguished by the pattern of aquaporin permeability. Dr. Jacques Benveniste claimed that water can remember the effects of a remedy, and that memory remains even after infinite dilution. This experiment confirmed the fact that homeopathic remedies change the properties of water. Further verification is required to determine whether this fact can be expressed as the memory of water. The memory of water claimed by Dr. Benveniste J. has been refuted by subsequent verification. However, homeopathic remedies remain very popular, especially in Europe. It may be possible to verify this effect by elucidating the properties of aquaporin permeability. Living organism life activities are affected by the type of water they drink. When mice were given natural mineral water with high aquaporin permeability, a clear change was observed in the aquaporin permeability of plasma water. The changes were maintained for 20 weeks while drinking natural water. They observed an increase in the amount of ATP in the organs of mice that drank water that was highly permeable to aquaporins, likely having a positive effect on the mice vitality. What is even more interesting is that it has become clear that the water in the cells of each organ is not the same. Water in brain cells is relatively permeable to AQP4. Water in kidney cells is relatively permeable to AQPs 2, 3, 4, and 5. Additionally, water in adipose tissue cells has relatively high permeability to AQP7. All organs in a mouse get their water from the blood. The difference in the type of water in cells depending on the organ may be influenced by the type of aquaporin distributed in the cells of the organ. Many studies have already revealed the types of aquaporins that are distributed in the cells of organs. AQP4 is distributed more in the brain than in other organs, as described by Nagelhus and Ottersen [9]. Many types of AQP are distributed in the kidney, as described by Matsuzaki et al. [13]. Furthermore, AQP7 is widely distributed in adipose tissue, as described by Lebeck [14]. In this study, we found that the relationship between the types of AQPs distributed in organ cell membranes and the water permeability within organ cells does not necessarily match. There is not only one type of AQP distributed in organs. In addition, fine separation of tissues was not possible in experiments on AQP permeability of water in organ cells. Therefore, another method will be required to elucidate the relationship between the types of AQP distributed in organs and the AQP permeability of water in the cells of the organs. It is possible to measure differences in aquaporin permeability at the cell level into which AQP-DNA has been recombinantly introduced, as described by Verkman [17], and using such a method will likely be able to elucidate this problem.

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