

# HEALTH BENEFITS OF ALKALINE IONIZED WATER Lim Khian Giap, Arunachalam Muthuraman<sup>\*</sup>

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# ABSTRACT

Water is one of the essential fluids in living organisms. The major characters of water area are colourless, transparent, odour free, taste-free, inorganic, and chemical substance. Alkaline water is a level of higher pH conditions than normal drinking water. Water treatment has a potential regulation of cellular systems. Besides, it shows pain relief actions on joints and supports themuscular strength by making muscular flexibility and joint movements. Alkaline water typically has a pH of 8 or 9. Alkaline ionized water is produced through the process of electrolysis of water. It has gained much research interest, particularly on its effects on human health. It was claimed that alkaline ionized water possesses radical scavenging properties and acts as anti-oxidant. This is due to the negative oxidation-reduction potential of alkaline ionized water. Most of the health benefits associated with alkaline ionized water is based on its anti-oxidative and radical neutralizing capacity. This article will discuss the health benefits of alkaline ionized water and the balance between acidity and alkalinity of the body.

Keywords: Alkaline water, Antioxidant, Radical scavenging, Ionized water, Oxidation-reduction potential.

# **INTRODUCTION**

Water is one of the essential fluids in living organisms. The major characters of water are a colorless, transparent, odour free, taste-free, inorganic, and chemical substance. It is major constitution of Earth's hydrosphere and the fluids of most living organisms. Alkaline water is a level of higher pH conditions than normal drinking water. Further, it is a vital part in the life and it doesn't provide calories and/or organic nutrients. Generally, alkaline water pH is higher than normal drinking water. Further, it produces the neutralization acid environment of the body. Naturally, normal drinking water is neutral and it has pH is 7. Aqua (water) therapy is involves a multiple like relief of joint pain and flexibility of joint movements. Alkaline ionized water (AIW) was initially produced in Japan and it is used in medicine as well as agricultural research to determine its value [1]. AIW has high hydrogen content, low oxygen content, and is characterized by high pH and low oxidation-reduction potential (ORP) [2]. Besides, it is shown that AIW possesses the ability to scavenge radicals. Hence, AIW becomes a subject of interest in research. This also led to more and more people are drinking AIW in Asia countries like Taiwan [3]. It is recognized to be effective in gastric hyperacidity, dyspepsia,

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### Dr. ArunachalamMuthuraman A

Pharmacology Unit, Faculty of Pharmacy, AIMST University, Semeling, 08100-Bedong, Kedah DarulAman, Malaysia diarrhoea, and normalizing gut microflora in Japan and Korea [4]. AIW is the water produced at the cathode in the process of electrolysis. It is also known as electrolyzed reduced water (ERW) [5]. AIW differs from alkaline water. In general, alkaline water can be produced by simply adding a basic substance like sodium bicarbonate into the water to adjust its pH to become alkaline. However, this is not the case in AIW. The higher pH in AIW is attributable to the enrichment of alkaline minerals and the removal of acidic minerals. Besides, it has smaller water molecules as compared to normal water [6]. The health benefits are only associated with drinking AIW that has undergone the process of electrolysis but not alkaline water. The following section is expressed the issue of bottled waters.

## **Bottled water**

Bottled water is one of the commonest sources of drinkable water. It was believed that bottled water is cleaner, purer, and has a better taste. It is also common for consumers to prefer bottled water as compared to tap water due to the apparent healthassociated with related risks tap water. Nevertheless, this is not the case for every bottled water. The reason behind this is companies may mix purified water with tap water and label bottled water as drinking water. The so-called "drinking water" usually only goes through the filtration process. In the market, there are plenty of options on the type of bottled water such as purified tap water, distilled water, treated underground water, drinking water, and AIW. All these types of water are confusing for consumers [7]. Further confusion can result as different companies employ different methods in the process of manufacturing and production of bottled water. Although bottled water is very essential, this industry is not carefully scrutinized as compared to that of the public tap water system. Hence, bottled water may not be pure. On the other hand, bottled water may not have a better taste as compared to tap water [8].

Another aspect that is a major concern regarding bottled water is the usage of the number 7 plastics to packaging the water. This type of plastic will degrade over time to release bisphenol A (BPA) [9]. A higher level of BPA in the human body is associated with a higher risk of cancer, central nervous system disorders, toxicity on the reproductive system, and altered immune system [10]. The usage of plastic bottles is not environmentally friendly. Plastic bottles are recyclable but each class of plastic requires special machines and processes. This does not only contribute to the complexity but also the cost of recycling plastic bottles. So, the used plastic bottles will turn out to be dumped in landfills. Since plastic is not biodegradable, more and more plastic will accumulate and cause pollution to the environment. especially when plastics are deposited in natural habitat like jungles and oceans. The animals will be harmed by eating the pieces of plastic and interrupt the natural ecosystem [11].

SI. No.	Characters	Descriptions
1.	Polymer	All other plastics including acrylic, fiberglass, nylon, polycarbonate and polylactic acid
2.	Resin identification code	Ê
3.	Abbreviation	Other
4.	Recyclability	Non-recyclable
5.	The time required for decomposition	Majority of these plastics never decompose; polylactic acid decompose in 6 months
6.	Toxicity level	High
7.	Most leached toxins	Bisphenol A (BPA) & Bisphenol S (BPS)

Table -1: Details of description and characters of plastics

### Health benefits of AIW

There is an increasing trend of evidence that claim the health benefits of drinking AIW in both animal and clinical studies. The health benefits associated with the consumption of AIW are based on its capability to neutralize and scavenge radicals present in the cells. AIW can prevent DNA, proteins, and other molecules against oxidative damage. Thus, it may play an important role in the amelioration of different disorders like cancer, diabetes, and renal impairment [12].

#### Antioxidants

There are many advantages associated with AIW in terms of human health. It offers enhanced hydration to the body, [5] ameliorates diseases like diabetes, and possesses anti-oxidative activity. Antioxidants can protect human cells and tissues against the damage done by certain molecules such as free radicals. Hence, they are not only able to minimize the risk of getting cancer but also prevent and fight against diabetes [13]. It is shown that AIW is effective in inhibiting DNA damage due to oxidative stress in vitro and in vivo [14].

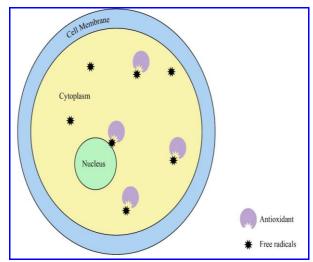


Figure- 1: Free radicals and antioxidants in a cell

## Reactive oxygen species (ROS)

ROS is nothing but any cation having one or more oxygen atoms.ROS is chemically reactive and participates in the process of oxidation. It is produced in the human body via biochemical reactions. However, when the ROS level in the human body is high, it will interact with other molecules like DNA, RNA, lipids as well as proteins and cause harmful effects [15]. Figure 1 shows the effects of ROS on cells. For example, ROS can damage DNA and increase the risk of developing cancer. ROS is associated with aging and many health disorders, for instance, hyperlipidaemia, liver inflammation, heart failure, ulcers, cancers, Alzheimer's disease, Parkinson's disease, and retinal degeneration [5,6, 16]. Oxidative stress refers to the extent of cellular damage caused by ROS. The oxidative stress of an individual is related to his lifestyle *i.e.*, cigarette smoking, alcoholism as well as prolonged exposure to the sun can raise the oxidative stress level above the physiological level. As mentioned above, ROS is produced via biochemical reactions that happen in the body and ROS plays a role in aging [3]. Following this, it was found out that the rate of aging is lower, and the lifespan increases when the intake calories were reduced while maintaining sufficient nutrition. This led to the postulation of reduced radical generation due to calorie restriction. This postulation is applied to an alkaline diet and AIW, where both can reduce the extent of oxidative damage in the human body [17].

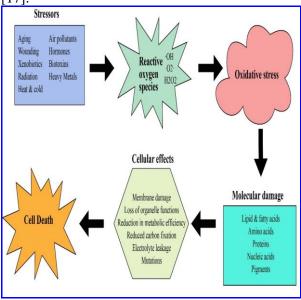


Figure 2: Flow chart of the effects of radicals on cells.

#### Oxidation-reduction potential (ORP)

ORP is the measure of the capacity of a substance to receive or donate electrons. In other words, ORP is the propensity of a substance to oxidize or reduce the other. The ORP value of any substance could be positive or negative. A substance with negative ORP value has the capability of neutralizing the ROS while a substance with positive ORP value is not capable of doing so [18]. The ORP value for normal tap water is between +200 to +600, which imply that it is unable to neutralize the ROS that is present in the body.In contrast, AIW contains more active hydrogen molecules and has negative ORP [19, 20]. Therefore, it acts as a reducing agent and can neutralize the ROS which leads to a lower risk of diseases [16]. AIW is produced through electrolysis of water. Both acidic and alkaline minerals are separated throughout the process and thus producing ionized water with high and low pH. The ionized water with a higher pH will look cloudier when it is dispensed out of the AIW machine. The AIW produced has high pH, low oxygen content, and high hydrogen content [21]. This can be observed as tiny air bubbles that are present in the water. The abundance of hydrogen offers health benefits as hydrogen is a very potent reducing agent and upon oxidation, it does produce unwanted oxidized products. The sooner one consumes the alkali ionized water; the higher the antioxidants level is present in the water. Therefore, it is recommended to drink the alkali ionized water within 6 hours upon dispensing to secure the health benefits [22].

In the process of generating AIW, the water molecules are broken into smaller size molecules. The water clusters in AIW comprise 4 to 6 water molecules but those in bottled water consist of 12 to 14 water molecules. As a result, they have a higher solubilizing capacity and greater permeability [6]. This is associated with easier and enhanced penetration of the water molecules into cells. Besides, ions such as calcium and magnesium are also found in AIW.Scientific researches showAIWcanneutralize and scavenge free radicals present in the human body [2]. In an in vitro study, it was found that AIWcan prevent and protect human lymphocytes DNA from oxidative damage done by hydrogen peroxide  $(H_2O_2)$ . Besides, the AIW can also diminish the extent of oxidative damage done by hydrogen peroxide  $(H_2O_2)$ . The protective effect conferred by AIW is not due to pH as alkaline buffer did not inhibit RNA oxidation. On the other hand, the AIW as well asaugments the antioxidant activity of ascorbic acid by oxidizing itself, thus preventing the ascorbic acid from being oxidized [23]. The figure below demonstrates the chemical reactions that happen during the electrolysis of water.

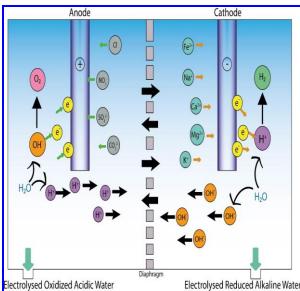


Figure- 3: Chemical reactions taking place in the process of electrolysis of water.

The electrolytic chamber consists of an anode, cathode, and a diaphragm. In the process, water molecules are ionized into hydroxyl (OH-) and hydrogen (H<sup>+</sup>) ions. All ions present in the water can pass through the semi-permeable diaphragm, where anions are attracted to the anode while cations are attracted to the cathode. At the anode, OH- ions donate electrons and are oxidized to oxygen gas. These electrons move to the cathode to be accepted by H<sup>+</sup> ions and are reduced to hydrogen gas. Both AIW and acidic ionized water are collected on each side at the bottom of the chamber. On the other hand, mineral nanoparticles, especially platinum nanoparticles are formed at the cathode. The platinum nanoparticles have a role in radicals scavenging and also activation of hydrogen atoms [24].

## Effects of AIW on cancer cells

Apart from making the hydration status of the human body better, AIW also promotes health in the long run. Owing to its antioxidant properties, it is capable of slowing down the rate of aging and prevent cancer by removing ROS in the body [2]. This was implicated by several studies. In a study by Nishikawa et al., in the year of 2005, the effect of AIW with platinum nanoparticles on murine Balb/c 3T3 cells transformation into cancer cells. The Balb/c 3T3 cells were given 3-methyl cholanthrene (MCA) prior to phorbol-12myristate-13-acetate (PMA), which acts as initiating and promoting substance. It was reported that the AIW with platinum nanoparticles suppresses the MCA/PMA induced transformation of Balb/c 3T3 cells. This is due to the absorption of platinum nanoparticles and hydrogen molecules into the cells. Then, the hydrogen molecules are

activated to scavenge the ROS within the cells and prevent the oxidative chain reaction [25]. In another study by Tsai et al., (2009), it was found that AIW possesses scavenging activity of ROS. When human leukemia (HL-60) cells were treated with reduced glutathione (GSH) together with AIW, the survivability of the HL-60 cells was significantly decreased as compared to that of cells given with GSH alone. This is the result of enhanced apoptosis that leads to the fragmentation of HL-60 cells DNA [26]. On the other hand, AIW was found to be effective in reducing intracellular ROS and lessen the liberation of  $H_2O_2$  from human lung adenocarcinoma cells. On top of that, the gene expression and secretion of vascular endothelial growth factor (VEGF) by human lung adenocarcinoma cells were diminished by AIW. Therefore, AIW can halt angiogenesis provoked by human lung adenocarcinoma cells [21].

## Effects of AIW in diabetes

In diabetes, oxidative stress is high due to increased production of ROS from protein glycation and glucose oxidation along witha reduction in the capacity of the antioxidant defense system. As previously mentioned, AIW helps to prevent and improve diabetes [3]. This is supported by several lines of evidence. In an animal study using type I and type II diabetic model, it was shown that the AIW has high potency in neutralizing radicals and reduces the blood sugar level isnot the only type I but also type II diabetic mice. With the administration of AIW, type I diabetic mice showed better insulin sensitivity while type II diabetic mice have a higher secretion of insulin on top of augmented insulin sensitivity [27]. In another animal study that uses type I (alloxan-induced) diabetic hamster, it was observedthat AIW can neutralize the radicals present in hamster pancreatic  $\beta$ -cells. Furthermore, it is capable of preventing the elevated cytosolic calcium ions level, escalation in DNA fragmentation, reduction of ATP level within cells, and disruption of insulin release in response to glucose that is associated with the damage done by alloxan [28].

## Effects of AIW in the renal system

AIW is also found to possess a protective effect on the renal system. In an animal study where cisplatin was used to induce kidney damage, pretreatment of animals with AIW resulted in a smaller extent of sodium, potassium, calcium, and magnesium increment in the urine as compared to the control group. Apart from that, the concentration of serum creatinine, blood urea nitrogen, and renal thiobarbituric acid-reactive substances are lower in the group treated with AIW relative to the control group. AIW treated showed higher activities of animals also antioxidative enzymes to the control group. These findings are supported by post-mortem histopathological studies [2]. On the other hand, Nakayama and his colleagues used AIW in haemodialysis (HD) of renal failure patients. They found that HD using AIW could avert the decrease in blood flow caused by dialysis. In patients suffering from peripheral arteriosclerosis, their skins were warmer during the treatment as compared to conventional HD. To add on, HD with AIW accelerated the healing of wounds in one of the patients with an ischemic lesion on his leg. All these effects observed are relatable to the anti-oxidative effect of AIW [29].

## Diet alkalinity and acidity to health

The physiological pH range where the human body functions optimally are from 7.35 to 7.45. That is to say, our body needs to have a slightly alkaline pH to be healthy. The human body is more likely to suffer from various diseases when the pH is always in the acidic range. For example, low body pH will increase the burden of the pancreas and impairs its ability to control the blood sugar level through insulin and glucagon. Impaired glucose homeostasis may increase the risk of an individual to suffer from diabetes [30]. High acidity also affects the calcium level regulation in the body where more calcium is extracted from the bones into the bloodstream. predisposing an individual to osteoporosis [31]. Therefore, it is crucial to maintain our body pH in a slightly alkaline range. This can be accomplished by consuming AIW. By maintaining a slightly alkaline pH, the above diseases can be avoided. Furthermore, our immunity will be optimized and this keeps our body away from various health issues [32]. Consumption of AIW is of great significance as about 70% of our body is made up of water. To purify regular tap water, chlorine was added. However, chlorine is harmful to our health and is reported to result in upper respiratory tract illness in children. Regular consumption of tap water will cause the chlorine to accumulate in the body and may affect the heart and digestive system [33]. By switching the consumption of regular tap water to AIW aids in the removal of toxins that are present in the human body, slow down the aging and deterioration of various disorders, and prevent diseases from happening. Since AIW is produced by electrolysis, the water molecules are split into smaller molecules and therefore, are easier to be absorbed by the cells to hydrate the body.

Apart from drinking alkalized ionized water, the body pH is also affected by diet to a great extent. Unfortunately, most of the foods and drinks that are favoured by most of the people are acidic in nature. These include fast food, processed meat, canned foods, sugar, flour, carbonated drinks, coffee, and sports drinks. Examples of food that provide alkalinity to the human body are bananas, sweet potatoes, spinach, cabbage, herbs, and many more [34]. The foods that belong to he acidic and alkaline category are depicted in Figure 4.To improve our health, it is essential to consume more foods that fall under the category of alkalinity. The consumption of fruits and greeny vegetables should be increased while the consumption of canned food, processed meat, and sugar should be reduced. Decent sources of fats like avocado, coconut oil, olive oil, and almond should not be ignored [35]. We can adapt these changes gradually instead of a complete change in eating habits within a short period of time. This way the efforts and goal towards the attainment of better health are more sustainable.



Figure- 4:List of acidic and alkaline food.

#### Miscellaneous uses of AIW

AIWis effective in removing stains on various surfaces and materials like carpet, baby clothes, curtains, carpets, tablecloths, and many more [36]. Generally, spray the AIW on the stain and add some cleaning agent. Then, allow some contact time and get rid of the stain with ease. Apart from stain removal, AIW can also serve as a disinfectant [37]. It can be applied to various household items *i.e.*, table tops, sinks, doorknobs, and kitchen utensils. Germs and bacteria can be eliminated by just spraying the surface to be disinfected with AIW and rub it with a clean dry cloth [38]. AIW not only able to disinfect household items but can also be applied to wash fruits and vegetables to remove pesticides that are present [39]. The bacteria can be removed by soaking them in AIW for few minutes, then discard the water and let them air dry. Baby

products, undergarments, toiletries can also be cleaned using AIW.

#### CONCLUSION

Although there is more and more evidence supporting the health benefits of AIW, there is no consensus on the consumption of AIW will result in health improvement. Hence, more researches in this area are needed. Besides, studies with better designs are warranted. The reason being many factors may impact the specific health outcomes of studies involving AIW, such as lifestyle, diet, smoking and alcoholism, genetics for some diseases, and settings. Nevertheless, AIW has a great potential to ameliorate or even prevent certain diseases or disorders and is worth further explore its effects and mechanisms in different health conditions.

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## Author's contributions

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### REFERENCES

- [1] RMC Ignacio, KB Joo, KJ Lee.Clinical effect and mechanism of alkaline reduced water, *J. Food Drug Anal*.20(1):394-397 (2012).
- [2] TC Cheng, YW Hsu, FJ Lu, YY Chen, NM Tsai, WK Chen, CF Tsai. Nephroprotective effect of electrolyzed reduced water against cisplatin-induced kidney toxicity and oxidative damage in mice, *J. Chinese Med. Assoc.* 81(2):119-126 (2018).
- [3] S Franceschelli, DM Pia Gatta, M Pesce, A Ferrone, A Patruno, MA de Lutiis, A Grilli, M Felaco, F Croce, L Speranza. New approach in translational medicine: Effects of electrolyzed reduced water (ERW) on NF-κB/iNOS pathway in U937 cell line under altered redox state, *Int. J. Mol. Sci*.17(9):1461(2016).
- [4] BD Pasiga, FH Akbar. Clinical effects of alkaline ionization water (AIW) as a mouthwash against the reduction of dental plaque, *Int. J. Appl. Pharm.*11(4):75-78 (2019).

- [5] J Weidman, RE Holsworth, B Brossman, DJ Cho, J St Cyr, G Fridman. Effect of electrolyzed high-pH alkaline water on blood viscosity in healthy adults, *J. Int. Soc. Sports Nutr.* 13(1):1-13 (2016).
- [6] K Masuda, Y Tanaka, M Kanehisa, T Ninomiya, A Inoue, H Higuma, C Kawashima, M Nakanishi, K Okamoto, J Akiyoshi. Natural reduced water suppressed anxiety and protected the heightened oxidative stress in rats, *Neuropsychiatr. Dis. Treat.* 13:2357-2362 (2017).
- [7] S. Drink. Bottled waters. In: PR Ashurst, R Hargitt, Soft drink and fruit juice problems solved, CRC Press, New York, 2017, pp. 145-160.
- [8] AFDijkstra, AM de Roda Husman.Bottled and drinking water. In: Y Mortajemi and H Lelieveld, Food Safety Management, Elsevier Inc., Amsterdam, 2014, pp. 347-377.
- [9] CS Kwan, H Takada. Release of additives and monomers from plastic wastes. In: H. Takada and HK Karapanagioti, Hazardous chemicals associated with plastics in the

marine environment. The Handbook of Environmental Chemistry, vol 78, Springer International Publishing AG, Cham, 2016, pp. 51-70.

- [10] M Murata, JH Kang. Bisphenol A (BPA) and cell signaling pathways, *Biotechnol. Adv*.36(1):311-327 (2018).
- [11] M Ilyas, W Ahmad, H Khan, S Yousaf, K Khan, S Nazir. Plastic waste as a significant threat to environment - A systematic literature review, *Rev. Environ. Health*33(4):383-406 (2018)
- [12] SK Park, JJ Kim, AR Yu, MY Lee, SK Park. Electrolyzed-reduced water confers increased resistance to environmental stresses, *Mol. Cell. Toxicol*.8(3):241-247 (2012).
- [13] M Henry, J Chambron.Physico-chemical, biological and therapeutic characteristics of electrolyzed reduced alkaline water (ERAW),*Water*5(4):2094-2115 (2013).
- [14] JS Lee, SK Park, SK Park. Electrolyzedreduced water mitigates amyloid beta toxicity via DAF-16 in *C. elegans, Toxicol. Environ. Health Sci.* 8(1):56-61 (2016).
- [15] T. Kashiwagi, H Yan, T Hamasaki, T Kinjo, N Nakamichi, K Teruya, S Kabayama, S Shirahata. Electrochemically reduced water protects neural cells from oxidative damage, *Oxid. Med. Cell. Longev.*2014:869121 (2014).
- [16] GV Frajese, M Benvenuto, R Mattera, S Giampaoli, E Ambrosin, R Bernardini, MG Giganti, L Albonici, I Dus, V Manzari, A Modesti, M Mattei, R Bei. Electrochemically reduced water delays mammary tumors growth in mice and inhibits breast cancer cells survival in vitro, *Evidence-based Complement. Altern. Med.* 2018:4753507 (2018).
- [17] M López-Torres, R Gredilla, A Sanz, G Barja. Influence of aging and long-term caloric restriction on oxygen radical generation and oxidative DNA damage in rat liver mitochondria, *Free Radic. Biol. Med.*32(9):882-889 (2002).
- [18] M Rajib, E Commission, M Parveen. A rapid technique for measuring oxidation-reduction potential for solid materials, *J. Sci. Technol. Environ. Informatics*7(1):510-516 (2019).
- [19] L. Bordoni, R Gabbianelli, D Fedeli, D Fiorini, I Bergheim, CJ Jin, L Marinelli, A Di Stefano, C Nasuti. Positive effect of an electrolyzed reduced water on gut permeability, fecal microbiota and liver in an animal model of Parkinson's disease,

PLoS One14(10):1-17 (2019).

- [20] Y Tanaka, Y Saihara, K Izumotani, H Nakamura. Daily ingestion of alkaline electrolyzed water containing hydrogen influences human health, including gastrointestinal symptoms, *Med. Gas Res.*8(4):160-166 (2018).
- [21] J Ye, Y Li, T Hamasaki, N Nakamichi, T Komatsu, T Kashiwagi, K Teruya, R Nishikawa, T Kawahara, K Osada, K Toh, M Abe, H Tian, S Kabayama, K Otsubo, S Morisawa, Y Katakura, S Shirahata. Inhibitory effect of electrolyzed reduced water on tumor angiogenesis, *Biological and Pharmaceutical Bulletin3*1(1):19-26 (2008).
- [22] T. Hamasaki, G Harada, N Nakamichi, S Kabayama, K Teruya, B Fugetsu, G Wei, I Sakata, S Shirahata. Electrochemically reduced water exerts superior reactive oxygen species scavenging activity in HT1080 cells than the equivalent level of hydrogen-dissolved water, *PLoS One*, 12(2):1-15 (2017).
- [23] MY Lee, YK Kim, KKRyoo, YBLee, EJ Park. Electrolyzed-reduced water protects against oxidative damage to DNA, RNA, and protein, *Appl. Biochem. Biotechnol*.135(2):133-144 (2006).
- [24] S Shirahata, T Hamasaki, K Teruya. Advanced research on the health benefit of reduced water, *Trends Food Sci. Technol*.23(2):124-131 (2012).
- [25] R. Nishikawa, K Teruya, Y Katakura, K Osada, T Kamasaki, T Kashiwagi, T Komatsu, Y Li, J Ye, A Ichikawa, K Otsubo, S Morisawa, Q Xu, S Shirahata. Electrolyzed reduced water supplemented with platinum nanoparticles suppresses promotion of two-stage cell transformation, *Cytotechnology*, 47(1-3):97-105 (2005).
- [26] CF Tsai, YW Hsu, WK Chen, YC Ho, FJ Lu. Enhanced induction of mitochondrial damage and apoptosis in human leukemia HL-60 cells due to electrolyzed-reduced water and glutathione, *Biosci. Biotechnol. Biochem.*73(2)280-287 (2009).
- [27] M Kim, H Kyung. Anti-diabetic effects of electrolyzed reduced water in streptozotocin-induced and genetic diabetic mice,*Life Sciences*79:2288-2292 (2006).
- [28] Y Li, T Nishimura, K Teruya, T Maki, T Komatsu, T Hamasaki, T Kashiwagi, S Kabayama, SY Shim, Y Katakura, K Osada, T Kawahara, K Otsubo, S Morisawa, Y Ishii, Z Gadek, S Shirahata. Protective mechanism of reduced water against alloxan-induced pancreatic β-cell damage: Scavenging effect

against reactive oxygen species, *Cytotechnology*, 40(1-3):139-149 (2002).

- [29] M Nakayama, S Kabayama, S Ito. The hydrogen molecule as antioxidant therapy: clinical application in hemodialysis and perspectives, *Ren. Replace. Ther*.2(23):1–10 (2016).
- [30] L Della Guardia, C Roggi, H Cena. Dietinduced acidosis and alkali supplementation, *Int. J. Food Sci. Nutr.*67(7):754-761 (2016).
- [31] GK Schwalfenberg. The alkaline diet: Is there evidence that an alkaline pH diet benefits health?, *J. Environ. Public Health*2012:727630 (2012).
- [32] A Lardner. The effects of extracellular pH on immune function, *J. Leukoc. Biol.*, 69(4):522-530 (2001).
- [33] I HarjanMohsen, A Harjan Mohsen, H Kamil Zaidan.Health effects of chlorinated water: a review article, *Pakistan J. Biotechnol*.16(3):163-167 (2019).
- [34] C Passey.Reducing the dietary acid load: How a more alkaline diet benefits patients with chronic kidney disease, *J. Ren. Nutr.* 27(3):151-160 (2017).

- [35] HAL Mousa. Health effects of alkaline diet and water, reduction of digestive-tract bacterial load, and earthing, *Altern. Ther. Health Med*.22(1):24-33 (2016).
- [36] M Stewart, A Bogusz, J Hunter, I Devanny, B Yip, D Reid, C Robertson, SJ Dancer.Evaluating use of neutral electrolyzed water for cleaning near-patient surfaces, *Infect. Control Hosp. Epidemiol.*35(15):1505-1510 (2014).
- [37] SME Rahman, I Khan, DH Oh. Electrolyzed water as a novel sanitizer in the food industry: Current trends and future perspectives, *Compr. Rev. Food Sci. Food Saf.* 15(3):471-490 (2016).
- [38] NS Meakin, C Bowman, MR Lewis, SJ Dancer. Comparison of cleaning efficacy between in-use disinfectant and electrolysed water in an English residential care home, *J. Hosp. Infect*.80(2):122-127 (2012).
- [39] J Hao, Wuyundalai, H Liu, T Chen, Y Zhou, YC Su, L Li.Reduction of pesticide residues on fresh vegetables with electrolyzed water treatment, J. Food Sci.76(4):3-7 (2011).