IHSA
H₂ standards

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Definitions and Standards on Hydrogen Measurements and Certifications

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Introduction

Currently throughout the world, biomedical researchers and the public are learning about molecular hydrogen therapy, including hydrogen gas inhalation, hydrogen-infused water (hydrogen water), etc. for the prevention of various diseases and overall health and wellness. The efficacy of molecular hydrogen is based on published scientific research. However, there has currently been no definition or standard, by the scientist or the public, of what constitutes a hydrogen product for therapy in terms of concentration, dose, or other requirements.

This situation has led to confusion in the industry, media, government, and commercial markets about hydrogen products. Since molecular hydrogen is a colorless, odorless, and a tasteless gas, it is difficult for the consumers to determine the concentration, or even the presence of molecular hydrogen in these products.

Therefore, scientific experts on hydrogen medicine from around the world have united together to discuss and define the international standards of molecular hydrogen. We established the International Hydrogen Standards Association (IHSA) in September 2016. These definitions and standards by IHSA will help advance the scientific research among academic and the medical community, provide guidance to governmental agencies, encourage responsibility in the hydrogen industry, and provide protection for the consumer.

In this document, IHSA specifically defines hydrogen water as water or liquids containing dissolved molecular hydrogen, which is termed by the chemical formula H_2. This document outlines the current definitions and recommended IHSA certification standards for hydrogen water, dated on September 14, 2017. The certification will denote that a product has met the minimum standard criteria set forth by IHSA.

Methods for determining the hydrogen concentration

Gas chromatography (GC) will be considered the primary method for measuring molecular hydrogen. GC should be the most reliable method for specialists in chemical analyses. In brief this method requires the transfer of H_2 from the aqueous phase to the gas phase using a tightly closed vessel, where hydrogen concentration can be measured by GC. The standard operating procedure (SOP) for measurement by GC will soon be determined by IHSA to mitigate systematic errors.

IHSA will also adopt a secondary method using an electrode that is specific to hydrogen. Several electrodes are currently available commercially; however, each has merits and shortcomings. Thus, one electrode will be carefully selected for the measurement, and the standard operating procedure (SOP) determined by IHSA. There may be other suitable options for general consumer use, but not for IHSA certification use. For example, IHSA may recommend different brands of electrodes, sensors, use of approved redox titration reagents, etc. However, methods that depend on using the oxidation-reduction potential (ORP) to estimate hydrogen in water are discouraged. Although a negative ORP is one of the characteristics of hydrogen water, ORP itself does not show the hydrogen concentration. Thus, ORP should not be used as a method to measure the hydrogen concentration.

The unit of measure for hydrogen concentration

IHSA will use the unit of milligrams per liter (mg/L) and not parts per million/billion (ppm/ppb) when discussing the concentration of hydrogen in water. This will help reduce the confusion from the multiple uses. For example, ppm can be used in chemistry as a mass (wt/wt), a mole (mol/mol), a volume (vol/vol), or weight/volume (wt/vol) fraction. Similarly, in physics, ppm can be used as proportional phenomena of length (α = 1.2 ppm/°C), or uncertainty in measurements (accuracy =1 ppm), or the chemical shift in spectroscopy (2 ppm). Additionally, the billion in ppb, may mean different values to different countries (10^9 or 10^{12}). Moreover, ppm is not recognized by the International System of Units (SI) and thus not an SI-compliant expression, and the ISO recommends against their use. Thus, for the IHSA standards and certification, milligram (mg) and milligram per litter (mg/L) are adopted as a dose and a concentration of hydrogen, respectively.

Concentration/dose

After much debate and consideration, IHSA suggests that the minimal amount of hydrogen should be established as a dose per day in a maximal volume of solution. The standard has been determined to provide at least 0.5 mg of H_2 by ingesting a maximal volume of 1 L of product water, or 500 mL of specialty beverages.

It is understood that more research is needed to fully know the minimum effective dose (MED) and the minimum effective concentration (MEC) of H_2 at the cellular level. Ideally, the dose would be given in mg/kg of body weight with an optimal time factor based on its half-life and pharmacokinetics/pharmacodynamics. However, this is more challenging with H_2 because unlike conventional pharmacological agents, H_2 does not have single/specific receptor/target or organ function. The MED/MEC will likely vary based on age, body weight, disease, genetics, intestinal bacteria, diet, etc. The IHSA recommendation is simply a standard based on the current cell, animal, and human clinical studies. It is not perfect and is subject to change based on additional biomedical research.

Supporting evidence

As noted by the Molecular Hydrogen Foundation/Institute (LeBaron T. W. 2015), human studies generally provide between 0.5 mg to 1.6 mg or more per day. This observation has been used as the basis for MHF's, and subsequently the Korea Water Society's recommended "target range" to the public. Here the scientific literature is evaluated the to justify a minimum hydrogen standard.

Unlike conventional drugs, it is logical that humans may require a similar equivalent dose of H_2 as do rodents because there are no receptors to bind H_2 as there are for drugs. The IHSA standard of a minimum of a 0.5 mg dose per liter of water is supported by the lower-dose studies in animals and humans. For example, in a mouse model of Parkinson's disease, Fujita, K. et al (2009) reported that a concentration of 0.08 mg/L, but not 0.04 mg/L was effective. Interestingly, mice (C57BL/6J) drinking 0.08 mg/L would provide a dose of H_2 per day which is somewhat comparable to a human ingesting about 0.5 mg of H_2 per day (0.08 mg/L * 0.0045 L/0.03 kg =0.012 mg/kg. 45-75kg = 0.5-0.9 mg H_2). Similarly, a 0.04 mg/L would equate to about 0.27 mg to 0.45 mg H_2 per day in humans. These doses are in line with two human studies that suggest that 0.5 mg, but not 0.25 mg per day is effective.

In one human study (Ito, M. et al. 2011), subjects ingested 0.25 mg/day by drinking 0.5 L of 0.5 mg/L H_2 water. At this low dose, there were no observed benefits. The researchers suggested that if they either a) consumed the same amount of water at a higher concentration, or b) consumed a higher volume of water at a similar concentration, then they would have noticed a benefit. Indeed, the preliminary data (open-label trial) in the same article, used 1 L of water (0.5 mg H_2 per day), and significant benefits were observed (only 0.5 L were consumed in the placebo-controlled trial because patients struggled to consume 1 L per day). However, another explanation could be the longer duration of the open-label study, which lasted 12 weeks instead of only 8 weeks. Another human study provided 0.5 mg H_2 per day by ingestion 1 L of 0.5 mg/L, and noted significant benefits (Song G. et al. 2013).

Dose instead of concentration

Setting a specific concentration (e.g. 0.8 mg/L) does not take into consideration the actual dose delivered due to the potential of different volumes ingested. For example, a higher dose of hydrogen can be ingested by drinking 1 liter of 0.5 mg/L, than could be ingested by drinking a 250-mL container of 1 mg/L H_2 water (i.e. 0.5 mg vs. 0.25 mg). Therefore, the IHSA standard is based on dose, and not concentration.

Volume

Although one can reach 0.5 mg of H_2 by ingesting a large volume of low concentration H_2-water (e.g. 5 L of 0.1 mg/L), this is problematic because: 1) some have difficulty drinking high volumes of water, and 2) it is possible that ingesting H_2 in this manner may not result in equivalent therapeutic effects as would ingesting 0.5 mg at once. This may be because the cellular concentration may not reach the "unknown" minimal required concentration (e.g. 5-10 μM). Additionally, the therapeutic effects of H_2 are not only dependent upon the dose/cellular concentration, but also on the frequency/exposure time. For example, continuous inhalation of H_2, or administration of non-digestible carbohydrates (e.g. lactulose), would provide a dose of H_2 orders of magnitude greater than that of drinking hydrogen water. However, only drinking hydrogen water, and not continuous hydrogen inhalation or lactulose administration was effective an animal model of Parkinson's disease (Ito, M. et al. 2012). This further illustrates the need for more scientific research to elucidate the optimal doses, timing, and methods of administration.

Based on the above human studies, and current guidelines for ingesting water, we have set the maximal volume as 1 L per day for water and 500 mL per day for specialty beverages (e.g. juice, carbonated drinks, teas, etc.).

Certification Criteria

Packaged hydrogen water:

1) provides at least 0.5 mg per 1 L serving
    a. minimum concentration is 0.5 mg/L
    b. drinking 1 L of water is practical for most people
2) passes safety test for toxins/heavy metals
3) maintains minimum concentration of 0.5 mg/L
    a. until the stated expiration date
    b. or for at least six (6) months if not stated
4) pH must not exceed 9.5
5) no false or damaging marketing claims that could harm the credibility of the hydrogen research and industry

Specialty beverages:

1) provides at least 0.5 mg per 500 mL serving
    a. minimum concentration is 1 mg/L
    b. drinking more than 500 mL of a H_2-rich beverage may not be recommend for health
    c. however, each beverage will be evaluated on a case-by-case basis.
        i. If an H_2 product contains stimulants or other potentially harmful ingredients where even 500 mL is too high of a volume.
2) passes safety test for toxins/heavy metals
3) maintains minimum concentration of 0.5 mg/L:
    a. until the stated expiration date
    b. or for at least six (6) months if not stated
4) pH can range from 3 to 10
5) no false or damaging marketing claims that could harm the credibility of the hydrogen research and industry

Hydrogen-water generating devices:

1) provides at least 0.5 mg per liter serving regardless of source water composition being used in the device (e.g. RO water or mineral water with a pH range of 5.8 to 8.6, current water guidelines)
2) passes safety test for toxins/heavy metals
3) produces the minimum concentration of 0.5 mg/L (either a and/or b):
    a. for the duration of the manufacture warranty
    b. for at least 1 year if not stated (this may be given in "cumulative operating hours)" not calendar time.

4) pH must be in range 5 to 9.5 regardless of source water composition (e.g. RO water or mineral water with a pH range of 5.8 to 8.6)
5) no false or damaging marketing claims that could harm the credibility of the hydrogen research and industry

Examples

A product can meet the standard of 0.5 mg per liter in many ways. For example, each product simply needs to provide a 0.5 mg dose by ingesting a maximum of 1 L of said product. Any volume less than 0.5 L would require a minimum concentration of 0.5 mg/L as explained below.

A 250-mL can at 0.5 mg/L would only provide 0.125 mg of H_2 per can. However, by ingesting one liter (1 L) of the product (i.e. four cans), the total provided dose of H_2 would reach 0.5 mg. Thus, the manufacture should recommend drinking 4 servings per day on the label. Similarly, a 500-mL serving at a concentration of 0.5 mg/L would only provide 0.25 mg of H_2 per serving. Ingesting 1 L of the product would provide the required 0.5 mg of H_2, and the manufacture would recommend at least two servings per day. Additionally, if a product provides a concentration of 0.8 mg/L with a volume of 750 mL, the manufacture still needs to recommend drinking 1 L per day (e.g. 1.34 servings).

Alternatively, if a 250-mL package had a concentration of 2 mg/L, then each serving would provide the required 0.5 mg of H_2, and only one can would need to be recommended. Similarly, a 500-mL serving at a concentration of 1 mg/L, would require the consumer to ingest 1 serving per day.

Lastly, products or hydrogen water devices whose concentration is less than 0.5 mg/L, and thus cannot provide a dose of 0.5 mg of H_2 per liter of product, cannot be certified

Additional products being evaluated by IHSA for certification standards:

- Hydrogen inhalation units
- Hydrogen cosmetics
- Hydrogen bath
- Hydrogen shower
- Hydrogen water generating additives (e.g. tablets)
- Oral ingestible hydrogen generating additives (e.g. pills)
- Other hydrogen generating methods

References

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