An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

A REVIEW ON WATER FOR PHARMACEUTICAL USE

Parameshwarappa Rajendra Patel*, M.P.Gowrav, Borra Vamsi

Pharmaceutical Quality Assurance Group, Department of Pharmaceutical,
JSS College of Pharmacy, JSS Academy of Higher Education & Research,
Sri Shivarathreeshwara Nagara, Mysuru, Karnataka-570015 India
*Corresponding author E-mail: praptel8626@gmail.com

ARTICLE INFO

Key Words
Drinking water, water for injection, Water storage and distribution system, Water Treatment.

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Water is a main component in numerous pharmaceutical and life-science activities. Water is commonly used as a raw material, component and solvent in the production, preparation and manufacturing of pharmaceutical drugs, active pharmaceutical ingredients (APIs) and intermediates. Maintenance of water quality during production, storage and delivery cycles like microbiology. Water may be used in a broad variety of applications, some of which involve intense microbiological supervision and others which do not need regulation. Pharmaceutical water treatment, storage and delivery facilities should be designed, installed, approved, accredited and maintained to ensure an effective supply of water of appropriate quality.Screening of conductivity, microbiological and chemical analysis of water used in pharmaceutical installations, calculate the capacity of a liquid to conduct electricity which correlates with the amount of dissolved salts (ions) in the solution, high ion counts, decreases water purity and may indicate a processing problem.Total organic compounds (TOC) testing tests how the carbon in the sample is held below the defined level of 500 parts per billion (ppb); bio-burden testing estimates the sum of micro-organisms in a water sample; microbial water testing includes calculating the quantity of viable aerobic bacteria present in a given water material.

INTRODUCTION

Water is clear and colorless substance and its main components for the source of water are lakes, sea, earth streams and oceans. This water fluid contains some of the living organism. Chemical formula of water is **H2O,** and it contain one molecules of oxygen and two molecules of hydrogen atoms are bonded covalently. The states of water are existing as liquid, solid and gases. It appears as iceberg, snow, fog and clouds due to atmospheric humidity. 70% of the earth surface is occupied by water and water present on the surface of earth undergoes water cycle through evapotranspiration. Water is natural resources utilized by living organism and other domestic purpose, it composed of various chemical substances which it is widely used in industries and also utilize for cooking and washing. In pharmaceutical industries it is mainly used as diluents, raw materials for the production of Active Pharmaceutical Ingredients (API). [1]

Water sources

Shallow water:

Water of such depth that bottom topography ha s a noticeable effect on the surface waves. It us ually means a depth of the water equal to less t han half the wavelength.

Ground water: This type of water present under earth's surface in pore space of rocks and breakages of rock development. Below the water table the ground water also flow with in there aquifers. The study of circulation and motion of underground water is called as hydrogeology. Under groundwater is often thought of within the similar terms as shallow water: inputs, outputs and loading. The essential distinction is that due to its low speed amount of turnover, underground storing is usually a lot of higher (in volume) related to inputs than it's for shallow water.

Freezing water: Water is convert it ice as a solid state depends on the impurity present in the water such as air bubbles and soil, it can seem transparent bluish-white in color. This type of frozen water is widely used for research purpose.

Water and waves: Sea and oceans comes under this category and about 4% of salt on average present in sea including some of the extraneous particles. Sea water is denser compared to freshwater. About -1.9℃ temperature seawater get freeze, as the concentration of salt increases the freezing point of the seawater decreases.

Upland Lakes and reservoirs: Typically situated within the source of stream systems, upland reservoirs area unit sometimes sited higher than any human habitation and will be encircled by a protecting zone to limit the opportunities for contamination. Bacterium and microorganism levels area unit sometimes low, however some bacterium, algae are going to be present in lakes. Wherever uplands area unit wooded or vegetable matter, soil acids will color the water. Several upland sources are having low pH which needs adjustment.

Rivers and canals: Low land water has a substantial microbial load and also presence of algae with a spread of dissolved constituents and suspended solids. A new technique of producing purified drinking water is done through extracting water from the atmospheric air and further cooling and condensing the water vapor. [2]

Characteristics of water: Water is an inorganic compound and polar in nature, it is odorless and colorless liquid. Density about 1 g/cm3, boiling point about 100℃, melting point about 0℃ and International Union of Pure and Applied Chemistry (**IUPAC**) name is oxidane.

1. **Physical characteristics**

   Some of the physical characteristics are

   1) Water turbidity,

   2) Color,

   3) Taste and odor,

   4) Water temperature,

   5) pH,

   6) Electrical conductivity

A) Water turbidity: Turbidity rod or turbidity meter is used for calculating turbidity by visual inspection and functional suspension is represented by mg / l or ppm and water turbidity is conveniently determined by turbidity rods and is constructed of aluminium. The turbidity meter it operates on the theory of measuring the intrusion by passing light rays emitted by the water sample.

B) Color: The standard color is formed by 1 mg of platinum cobalt is dissolved in water(1L) then on the cobalt scale color number should not more than 20 and should be less than 10. Tintometer is the instrument used to determine the color of water.

C) Taste or odour: The intensity of the odor is used to measure the magnitude of the odor present in the particular water sample, it is related to the odor threshold.

D) Water temperature: Temperature for portable water is about 10℃ is desired and it should not exceed more than 25℃.

E) Specific conductivity: Estimation of individual water conductivity is

determined by assessing the amount of dissolved salt found in water.

Chemical characteristics

1. Total amount of solid and solid suspended in water. The solid substance attained by evaporating a water sample and remaining dry residue is collected on the filter paper and weight the amount of residue remained in it.
By filtration method the suspended solid is separated from the water sample. The limitation for the total amount of solid permissible is 500 ppm.

Water hardness- Water hardness is undesirable because it leads to formation of corrosion, more consumption of soap, coating of pipes, tasteless food etc. Temporary hardness: if magnesium and carbonates of calcium are present in water it leads to formation of hard water, this hardness can be removed by some extent of simple boiling or by adding lime to water for longer extent. Such type of hardness is called temporary hardness.
Permanent hardness: if chlorides, magnesium and nitrates of calcium are in water it leads to permanent hardness, it cannot be removed by simple boiling. This type of water requires some standard treatment for water softening.
Chloride content: Water containing chloride is to be measured by titration method, water is titrated with standard silver nitrate solution is used and indicator as potassium chromate.
Biological oxygen demand (BOD): The amount of organic matter existing in water sample is calculable by passing an amount of oxygen to the sample and identifies the oxygen utilized by the organic matter existing in water. This demand is known as Biological gas demand (BOD).[3]

The purpose of water for pharmaceutical industry: Water is regularly used as raw materials, medicines and other medicinal applications very frequently, and also for washing purposes such as appliances. Water quality is very essential and should be free of chemical, inorganic impurities and microorganisms because it is commonplace to disperse or grow microorganisms in water and can influence them through water distribution and storage.

The grades of water listed for better acceptance in pharmaceutical use under USP, and also exp ress the standard characteristics for pharmaceut ical development according to its specificity.

1. Potable water

2. Purified water

3. Water for hemodialysis

4. Water for injection

5. Sterile water for injection

6. Sterile water for inhalation

7. Sterile water for irrigation

8. Bacteriostatic water for injection [4]

Water storage and distribution system: The distribution and storage of water is conside red to be a key part of this whole system, and th e strategy is to be totally combined with the wa ter distillation components of the system.Water comes under major commodities in pharmaceu tical industries. It is used as an excipient and us ed for yield reform during the synthesis process , at the final stage of production or for cleaning equipment, vessels etc.[5]

Water Treatment- It can be categorized by environmental treatment progress operation is used; example like physical, chemical and biological.

Water treatment process - Physical methods

These involve processes wherever there is no a pparent chemical or biological process change and severe physical phenomena are involved in the improvement of water. For example, the us e of coarse separate screening is to remove larg er substances and sedimentation.

a) Coagulation and flocculation

The first step is the conservative method of distillation of water, which involved the concentration of chemicals to facilitate the removal of particles found in water. Inorganic particles such as cut, clay, etc., or organic particles such as protozoa, algae and viruses, etc., lead to the formation of turbidity and water colour.

Sedimentation: The physical phenomena with respect to the subsidizing of solids by square gravity measure allowed control in the sedimentation process. It typically consists of simply holding the water in a tank under inactive conditions for a short amount of time, enabling the denser solids to settle down, and removing the "clarified" effluent.

Filtration: After most flocculous dissociation, t he water is purified because the final step is to get rid of leftover suspended components and u nsettled flocculus.

b) Rapidsand filters

Rapid sand filters are the widely used filters a nd vertically moving water through sand that often create a higher layer of C or coal than th e sand. The upper layer discards the organic matter, leading to smell and taste.

c) Membrane filtration

Drinking water and sewage water filtration i s commonly treated by membrane filters. Un like cryptosporidium and giardia, the particl es greater than 0.2 um are also filtered using membrane filters.

1) Chemical treatment

This increases water quality by requiring che mical reaction in the water. Chlorination is th e most common method used in processing ch emicals.

Chlorination: Water chlorination is a process b y which chlorine compounds such as sodium h ypochlorite are added to water. It is a strong oxi dant and therefore leads to a rapid killing of har mful microorganisms. These are highly toxic g ases, which prevent the spread of some waterbo rne diseases such as cholera, typhoid and dysen tery.

Ozone disinfection:

Ozone is known as an unstable molecule that d elivers one atom of O promptly, providing a str ong oxidization that is virulent to most waterbo rne species. It is an effective technique to inacti vate harmful protozoa that cysts.

Neutralization:For manufacturing, the chemic al process used for water treatment process is c alled neutralization. Neutralization involves ad ding acid or base to control pH levels back to e quilibrium. Because lime can be a base, it is co mmonly used in waste acid neutralization.

Biological treatment methods: This method uses micro-organisms, mainly bacteria, to create stable end products in the biochemical decomposition of wastewater. Biological treatment strategies can usually be classified into aerobic and anaerobic procedures, depending on the dissolved oxygen required. Although the wastewater treatment systems are complex and can definitely include physical, chemical and biological solutions, they can all be grouped under six methods in general: This treatment is used for microorganisms, widely used for bacteria,

1. Preliminary Treatment,
2. Primary Treatment,
3. Secondary Treatment,
4. Disinfection,
5. Sludge Treatment,
6. Tertiary Treatment [6]

TYPES OF WATER

1) **Hard water -** Due to the acidic rain hard water is produced. The rain dissolves rocks into the mud, creating hard water. Hard water originates from the soil and is usually taken from a well or spring. The water is purified by passing over rocks and collecting minerals from them, such as lime, magnesium and calcium.The high mineral content is the explanation for its better taste and it is even said to be better for your health as the National Research Council states that it can be used as a dietary supplement for minerals like calcium and magnesium.
2) **Soft water-** Soft water is collected from the surface, as has been collected from lakes, rivers and rainwater. Soft water is typically high in sodium but has a small concentration of calcium and magnesium unlike hard water. It is because of the difference in mineral content that makes soft water better for your skin because it is not dried up by the minerals.[7]

Drinking water - One can refer to drinking water as potable water. Drinking water must meet either the NPDWR's quality attributes, or the European Union or Japan's drinking water regulations, or the WHO Drinking Water Guidelines. It can be obtained from a variety of sources including a public water utility, a

private water supply (e.g., a well) or a combination of those sources

Purified Water - Purified Water is used as an excipient in the manufacture of non-parenteral formulations and other pharmaceutical uses, such as the washing of parenteral product-contact parts of certain devices.Purified water must meet requirements of ionic and organic chemical purity, and must be shielded from microbial contamination. Drinking water is the source or feed of Purified Water for producing. Also, it should be protected against microbial replication and recontamination.

Highly purified water - Highly purified water (HPW) should be treated as a minimum quality feed-water from drinking water. Highly filtered water reflects a special water standard found only in the European Pharmacopoeia. This grade of water must follow the same quality standard as injection water (WFI), including the endotoxin cap, but the water treatment method used may differ. For example, current production methods include double pass RO coupled with other appropriate techniques such as ultrafiltration and deionization. HPW can be prepared using a combination of various methods such as RO, ultra-filtration and de-ionization. Highly purified water (HPW) from drinking water will be handled as a low grade feed-water. Highly purified water represents a specific quality for water contained only in the European Pharmacopoeia. Such water classification will meet the same consistency level as injection water (WFI), including the endotoxin cap, although the process used for handling water can vary. For example, recent processing processes require double pass RO combined with other relevant strategies such as ultrafiltration and de-ionization. HPW can be treated with a mixture of various methods including RO, ultra-filtration and de-ionization.

Water for Injection- Water for injection (WFI) is being used as an excipient in parenteral production and other formulations where the drug's endotoxin content must be controlled, and in certain medicinal uses, such as the washing of other devices and parenteral direct-contact materials. Drinking water (usually with additional treatment) or filtered water as a minimum should be prepared for injection.[8]

COMMON METHODS OF WATER PURIFICATION

Boiling - It is certainly the safest approach, but petroleum reserves or natural resources are also inconvenient and inefficient. Water should be kept boiling for minutes continuously, which at any altitude is sufficient. When cooling, the water needs to be filtered to avoid recontamination and should taste better as well.

Filters and pumps- There are now several water purification devices available but care must be taken in choosing the right one for your expedition. Most systems use a simple method of filtration, by which water is pumped into tiny holes through which organisms can not move. Be careful to look at the size of the pores (measured in microns), since anything greater than microns will not eliminate all organisms. Some systems use a filter as well as a chemical procedure that strains and sterilizes in one go.Choosing the right device is important, so here are some tips:

- Producers also tell how many liters of pure water a product contains. But if the water is silty, this can be significantly decreased.
- Make sure that the purifier can be removed, cleaned and reassembled in the field to avoid blockages if heavy usage is anticipated.
- Test the pump rate, as some can require a great deal of energy to generate a small amount of water.
- Most pump makers go to great lengths to say what they're going to take away while remaining quiet on what's not taken away. Of starters, without the introduction of a carbon filter, pumps do not extract chemical effluent, such as mercury in the Amazon tributaries. In those places of visit where the Water treatment period is also important; the water should preferably be used within hours of sterilisation.

Water Purification Technique for Pharma Industry

Steam distillation: Steam distillation is a special distillation method (a separation process) for materials sensitive to temperature, such as natural aromatic compounds. It was once a common method of purifying organic

compounds by laboratory, but it has become obsolete by vacuum distillation. Steam distillation remains relevant in some segment of the industry. Most organic compounds tend to decompose at high temperatures which are maintained. Separation by distillation at usual boiling points (1 atmosphere) is not an option, so water or steam is added into the distilling apparatus.

Fractional distillation: Fractional distillation is the division of a mixture into its component parts or fractions, which distinguishes chemical compounds by their boiling point by heating them to a temperature at which one or more fractions of the compound are vaporized. This uses for fractionation distillation. The component parts usually have boiling points that vary under a pressure of one atmosphere from each other by less than 25 ° C. Usually a quick distillation is used when the difference in boiling points is greater than 25 ° C.

Pot still: A pot is either a distilling device when used to distill distilled spirits such as bourbon when cognac. Pot stills operate on a batch distillation basis (as opposed to a Coffey or column stills which operate continuously). Traditionally constructed from copper, pot stills are made in a number of shapes and sizes, depending on necessary quantity and form of spirit.

Vacuum distillation: Vacuum distillation is a distillation process by which the pressure to be distilled above the liquid mixture is lowered to below its vapor pressure (usually less than the atmospheric pressure) which allows the most volatile substance to evaporate. (The one with lowest boiling points). This method of distillation operates according to the theory that when the vapor pressure of a liquid boils

Distillation: Distillation is a process by selective evaporation and condensation which separates the component or substances from a liquid mixture.Distillation may result in substantially complete separation (nearly pure components), or selective separation may lead to an increase in the concentration of chosen mixture components. The distillation has many uses for industrial purposes. For examples: Distillation is a major class of process in the fossil fuel industry in acquiring crude oil materials for fuels and chemical feed stocks. Distillation enables air to be segregated into its constituents • especially oxygen, nitrogen and argon for industrial use. In the area of industrial chemistry, wide ranges of chemically synthesized natural liquid products are separately distilled

Reverse Osmosis- Semi-permeable membranes are used in reverse osmosis processes. Alternatively, RO membranes ' "pores" are inter-segmental spaces between the polymer molecules. They are wide enough to penetrate water molecules but too thin to facilitate the passage of hydrated chemical ions. Nevertheless, the selectivity of this absorption is determined by several variables including pH, temperature and pressure differential across the membrane.Some issues related to the design and function of RO systems include highly sensitive membrane materials for sanitizing agents and particulate matter, chemical and microbial membrane foul; quality of membranes and seals; flow of dissolved gasses such as carbon dioxide and ammonia; and quantity of wastewater, especially where water discharge is tightly controlled by local authorities.Failure to preserve the integrity of the membrane or seal can contribute to liquid water pollution. Control procedures require sufficient pre-treatment of the effective water stream, appropriate range of membrane components, quality issues, membrane construction and heat resistance, frequent sanitization and control of differential strain, conductivity, microbial and TOC levels.

Deionized Water - Such water is created through an ion-exchange process in which either H+ or OH– ions replace the contaminating ions. As with Distilled Water,Deionized Water is mainly used as a solvent for the preparation of reagents, but is also defined in the efficiency of other test aspects, such as the transfer of an analyte as a reference standard or analytical blank as well as for the cleaning of test apparatuses.

Ammonia-Free Water - Functionally this water has to have a minimum ammonia content to avoid toxicity in ammonia-sensitive tests. It has also been equated with High Purity Water

and has, among other ions, a Phase 1 conductivity requirement and is marginally tighter than Purified Water due to the current latter's tolerance for a minimal ammonium standard. Unless, indeed, the Purified Water used by the user is purified and met or fulfilled the criteria for high pure water conductivity, it can contain nil ammonia or other ions and should be used instead of high pure water

Lead-Free Water - In a Lead 251 test this water is used as a transition diluent for an analyte. Although no specific instructions for its preparation are given, there must be no visible lead in it. Purified water should be an acceptable replacement for that water.

Activated Carbon - Granular activated carbon beds adsorb organic material with low molecular weight and oxidizing contaminants such as chlorine and chloramine compounds, which are extracted from the atmosphere. These are used to achieve other qualitative attributes and to guard against reaction with downstream materials, resins and membranes of stainless steel. Control measures may include control of water flow levels and differential pressures, hot water or steam sanitization, backwashing; adsorption power testing and regular replacement of the carbon bed Activated carbon is used in pretreatment to extract chlorine and chloramine from feed water so that it does not harm membrane filters and ion exchange resins. Most activated carbon is produced in the presence of water vapor and CO2 by "activating" the charcoal from coconut shells or coal by roasting at 800-1000 ° C. [9]

CONCLUSION

Various grades of water are used for various purposes at the pharmaceutical firms. To follow the guidelines for maintaining quality attributes, it is therefore necessary to know all the grades of pharmaceutical water, its preparation, specifications and usages.Within regulatory rules for pharmaceutical manufacturing facilities, water handling systems should be allowed by carrying out different quality checks for physicochemical and microbiological impurities.

REFERENCES:

1. Vishal Gupta. N. Water for pharmaceutical use. Int. J. Pharm. Sci. Res. 2015: 36(1): 199-204.
2. Different sources of water [internet]. Sciencing.com.2019. Available from. https://sciencing.com/different-sources-water-7624072.html
3. Characteristics of water- Physical, Chemical and Biological [Internet]. Theconstructor.org.2019.
4. Quality of water for pharmaceutical use: an overview [internet].pharmatutor.org.2019. from.https://www.pharmatutor.org/articles/quality-of-water-for-pharmaceutical-use-an-overview
5. Pharmaceutical water system: pharmaceutical water storage & distribution systemPharmawiki.in.2019. from.https://pharmawiki.in/pharmaceutical-water-systems-pharmaceutical-water-storage-distribution-systems-pdf-ppt/
6. Venkateswara Reddy. Water Treatment process in pharma industry- A Review. International journal of pharmacy and biological science.2014: 4:07-18
7. Hard water vs. soft water: which one is healthier?Internet].healthline.com.2019 https://www.healthline.com/health/hard-water-and-soft-water#Whats-the-difference-between-hard-water-and-soft-water?
8. WHO good manufacturing practice: water for pharmaceutical use[1] [Internet].who.int.2019. Available from.https://www.who.int/medicines/areas/quality_safety/quality_assurance/GMPWatePharmaceuticalUseTRS970Annex2.pdf?ua=1
9. Water purification: purification of water [internet].en.wikipedia.org.2019. From.https://en.wikipedia.org/wiki/Water_purification.