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A Study of the Physicochemical Properties of some Water Types Used in Solving the Syrups in Powder Form

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ABSTRACT

The aim of this research is to conduct analyses of physicochemical properties of some water types used in general in solving the syrups in powder form in Syria. Samples were taken from ordinary tap water, cooled and boiled tap water, bottled spring water, and ions-free water from three pharmaceutical companies in Syria.

The tests were performed to sample: pH, Conductivity, Density, Viscosity, Free Chlorine, Ammonia, Nitrite, Nitrate, Copper, Iron, Phosphorus, Sulfate, Fluoride, Bromine, Manganese, Sodium, Lithium, Potassium and Magnesium ions, In addition to the bacterial test.

The devices used for the analysis in this research are: HPLC, Turbidity meter, Conductivity meter, DR/890 Colorimeter, pH meter.

Results were computed according to the Syrian standards and the United States Pharmacopeia.

KEY WORDS: Water Physicochemical properties, Solving, Syrups, Ions, HPLC, Pharmacopeia, Powder.

1. INTRODUCTION

Water is the most important and the most prevalent component of plant and animal cells and its existence is linked to the existence of life. It is an appropriate compromise for the occurrence of most of biochemical reactions, and it has a role in thermal regulation at organisms because of the high thermal capacity (Kotz, 2005).

The chemical formula of water is H_2O. It is composed of two atoms of hydrogen and one atom of oxygen. Water molecules are linked to each other with bonded hydrogen. Water is a tasteless, odorless liquid at normal temperature and pressure, and it appears colorless in small quantities, although its own color is very light blue. Snow is also colorless, and water vapor is essentially invisible in the state of gas (Pop, 1996).

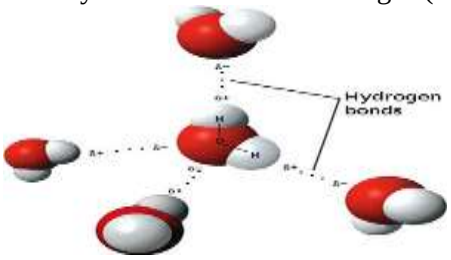


Figure.1. Shows the association of water molecules with hydrogen bonds

Water is a good polar solvent, usually referred to as general solvent. Soluble chemicals in water are known as hydrophilic materials, such as salts and sugars, acids, alkalis, and some gases such as oxygen and carbon dioxide. On the other hand, Insoluble chemicals in water are known as hydrophobic materials, such as fats, oils, organic compounds. (Kotz, 2005; Pop, 1996) Water mixes with many liquids, such as Alcohols (for example, ethanol, in all proportions).

In the Pharmaceutical Industry: Water is used as a solvent in Syrups, Lotion, Drops, Gargles and solutions in general. Water solves organic and mineral salts, acid and base and sugar materials. It has a little incompatibility with pharmaceutical substances but it repulses Aspirin and Barbiturates. Solutions in which water enters as a solvent with large amounts are called Aqueous Solutions (Allen, 2011; 2012; Mahato, 2012).

Water types used in the Pharmaceutical Industry:

Drinking water: It contains some salts, such as magnesium, sodium chloride, calcium, sulfate.

Distilled water: A pure water free of salts and impurities and bacteria, it is obtained by distillation and used to solve the drug substance on a large scale.

Double-distillation water: It is conducted by a double distillation process, and it is very pure and free of impurities and bacteria, it is used in the preparation of Injection solutions and serums.

Sterile water: It is distilled, free of impurities and bacteria and heat generators and Pyrogenic used in Injection solutions and serums among others.

Purified water by ions devices: It looks like a distilled water, it is free of impurities and salts but it may contain bacteria and heat generators.

Aromatic water: It is aromatic and distilled water, which has been used for a long times e.g. Rose water, mint water, camphor water.

Mineral water: It contains a large amount of mineral salts, such as calcium, sodium, magnesium and phosphate.

Characteristics of the water used as a solvent: It should be distilled and free of impurities, bacteria and oxidation and Reduction materials, tasteless, odorless. The degree of concentration pH is between 6-7.5 and it should be free of gases (oxygen and coal gas) (Allen, 2011; 2012; Mahato, 2012).
The final result: Water is an inert solvent. It doesn't interact with the drug substance, tasteless, odorless, and suitable for injection and internal use. It is an ideal solvent for the preparation of many pharmaceutical dosage forms.

2. MATERIALS AND METHODS

The following samples of water have been used: [Ordinary tap water (sample.1), boiled and cooled ordinary tap water (sample.2), bottled spring water (sample.3), Purified Water for three pharmaceutical companies in Syria (sample 4, 5, 6)]. The tests of the samples were performed at The Qadmous analysis laboratory of water. The results were computed according to the Syrian standards and the US Pharmacopoeia of the water used in the pharmaceutical industry.

Physical Analysis:

Sensory tests: These tests are conducted using the natural senses to determine the color and the taste and odour of the article. Pure water has no color, taste or odor, and it is a clear fluid without turbid.
Sample size: The size of the containers is verified, using laboratory available methods.
Leakage: The packaging is checked to make sure it was tightly closed and no leakage is possible.
pH: pH was measured using a (sens ion 1/pH meter) HACH device from the US HASH COMPANY. 100ml of sample water was taken in the clean and dry Beaker, then the electrode was placed in beaker, the device was turned on, then the value of pH and temperature were read on the device's screen.
Turbidity: Turbidity was measured using a (HI 93703/TURBIDITY METER) HANNA device. The device was turned on, the cell was filled with sample water, the cell was placed in the device compartment, then the turbidity value was read on the screen of the device with the NTU unit.

Electrical Conductivity, Total dissolved solids (TDS): The proportion of dissolved salts, Temperature: Electrical Conductivity, TDS, the proportion of dissolved salts, Temperature were measured using a HACH device (sens ion 5/conductivity meter) of The US HUSH COMPANY. 100ml of the sample water was taken in the clean and dry beaker, the device was turned on, then the electrode placed in beaker, the Conductivity value by µs\cm unit, Temperature value, the TDS value by mg/l unit, the value of the salts percentage sal% were read on the screen of the device.
Density: Density was measured using a pycnometer device.
Viscosity: Viscosity was measured using an Ostwald device.
Chemical tests: Free Chlorine was analyzed by chlorine color meter from HACH company with DPD Method: Chlorine in the sample as hypochlorous acid or hypochlorite ion (free chlorine or free available chlorine) immediately with DPD (N,N-diethyl-p-phenylenediamine) indicator to form a pink color which is proportional to the chlorine concentration.

Ammonia was analyzed by DR/890 colorimeter from HACH Company with Salicylate Method: Ammonia compounds combine in the presence of a sodium nitroprusside catalyst to form a blue-colored compound; the blue color is marked by the yellow color from the excess reagent present to give a final green colored solution.

Nitrite was analyzed by DR/890 colorimeter from HACH company with Diazotization Method (powder pillows): Nitrite in the sample reacts with sulfanilic acid to form an intermediate diazonium salt; this couples with chromotropic acid to produce a pink colored complex directly proportional to the amount of nitrite present.

Nitrate was analyzed by DR/890 colorimeter from HACH Company with Cadmium Reduction Method: Cadmium metal reduces nitrates present in the sample to nitrite; the nitrite ion reacts in an acidic medium with sulfanilic acid to form an intermediate diazonium salt which couples to genotypic acid to form an amber-colored product.

Copper was analysed by DR/890 colorimeter from HACH Company with Bicinchoninate Method: Copper in the sample reacts with the salt of bicinchoninic acid contained in CuVer 1 or 2 copper reagent to form a purple colored complex in proportion to the copper concentration; this method includes procedures for both powder pillow and AccuVac reagents.

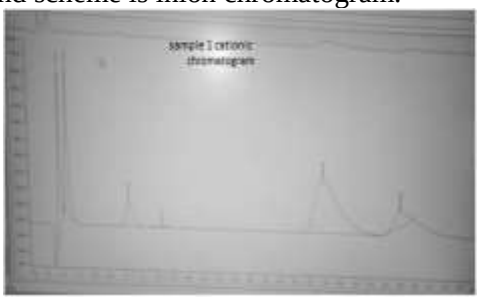
Iron was analyzed by DR/890 colorimeter from HACH Company with FerroVer Method: FerroVer iron reagent reacts with all soluble iron and most insoluble forms of iron in the sample to produce soluble ferrous iron; this reacts with 1, 10-phenanthroline indicator in the reagent to form an orange color in proportion to the iron concentration.

Phosphorus was analyzed by DR/890 colorimeter from HACH Company with Orthophosphate Method: Orthophosphate reacts with molybdate in an acid medium to produce a phosphomolybdate complex; Ascorbic acid then reduces the complex, giving an intensemolybdenum blue color.

Sulfate was analysed by DR/890 colorimeter from HACH Company with SulfaVer 4 method: Sulfate ions in the sample reacts with barium in the SulfaVer 4 sulfate reagent to form insoluble barium sulfate; the amount of

turbidity formed is proportional to the sulfate concentration; the sulfaVer 4 also contains a stabilizing agent to hold the precipitate in suspension.

Fluoride, Bromine, Manganese, Sodium, Lithium, Potassium and Magnesium ions were analyzed using 850/IC Ion chromatography device from the SWISS METROHM Company. This device was used to determine positive and negative ions with ion chromatography method at once without having to change the solvent and columns, this device gives results in the form of two chromatograms scheme, the first scheme is cation chromatogram while the second scheme is inion chromatogram.



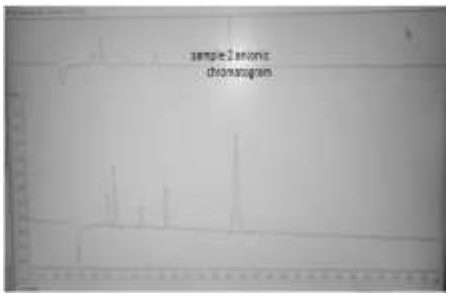


Chart.1. Shows a cationic chromatogram **Chart.2. Shows a anionic chromatogram**

3. RESULTS AND DISCUSSION

Table.1. Physico-Chemical analysis results

Test	Permissible values	1	2	3	4	5	6
Appearance	Clear colorless	Clear colorless	Clear colorless	Clear colorless	Clear colorless	Clear colorless	Clear colorless
Taste and Odour	Natural	Natural	Natural	Natural	Natural	Natural	Natural
Packagings		-	-	Sealed Plastic	Sealed Plastic	Sealed Plastic	Sealed Plastic
Written Size on the Packaging		-	-	500 ml	60 ml	60 ml	60 ml
Real size				540 ml	58 ml	59 ml	60 ml
Free Chlorine mg\l	0.5	0.22	-	-	-	-	-
Turbidity NTU	1	0.88	0.35	0.32	0.41	0.46	0.45
Density g\cm^3	0.998 at 20^{0}C	0.998	0.998	0.998	0.998	0.998	0.998
Viscosity c.p		0.825	0.825	1.049	1.118	0.945	1.022
pH	5-7	7.69	7.10	7.68	6.92	6.91	6.93
Conductivity	25	403	528	365	12.82	10.42	9.17
TDS mg\l	15	194.3	256	175.7	5.6	4.6	3.9
Temperature ^{0}C		10.9	10.6	10.3	14.0	14.0	13.9
Sal %	0.004%	0.20	0.30	0.20	-	-	-
Chlorine mg/l	0.5-1	9.75	0.630	0.63	0.258	1.130	1.300
Ammonia mg/l	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Nitrate mg/l	0.2	12.3	8.1	8.7	6.1	0.31	6.2
Nitrite mg/l		0.021	0.024	0.025	0.008	0.008	0.003
Phosphate mg/l	0.01	0.09	0.024	0.025	0.01	0.01	0.01
Copper mg/l	0.01	0.04	0.05	0.06	0.01	0.01	0.01
Iron mg/l	0.01	0.00	0.00	0.48	0.00	0.00	0.00
Fluoride mg/l		0.972	0.110	0.330	0.172	0.180	0.175
Bromine mg/l		0.981	-	0.08	-	-	-
Sulphate mg/l		48	45	17	0.163	0.04	0.154
Maganese mg/l	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Lithium mg/l	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Sodium mg/l	0.68	8.73	4.11	0.141	1.407	0.141	1.33
Potassium mg/l	0.1	8.80	6.25	13.27	-	-	-
Calcium mg/l	1	14.12	5.2	7.3	1.46	1.35	0.73
Magnesium mg/l	0.1	7.29	5.07	1.3	0.137	0.13	0.122

Bacterial test: The Membrane Filters Technology (MF): This method involves the filtering of 100ml of sample water by using a pump on a sterile filter with a 0.45mm pore size which retains bacteria in the water on its surface (filtration technique by vacuum Pressure), it has been put the sterile filter on a selective medium, then it has been placed the filter with the medium in the incubator for 72 hours at 37.5^0C. (Used Incubator name: Memmert cat.21076.00.500).

Bacterial culture medium has been used in this research: AGAR DE Chapman TTC ISO 9308-1, which is particularly detecting Coliform and Escherichia coli, the bacteria appear bright yellow or bright green color if there are bacteria in the water.

How to prepare the bacterial medium: Weigh 56.2gm of cultured material, solve it in 1000 ml of distilled water by heating until complete dissolution with stirring gently, then Sterilize the solution for 15 minutes at 121^0C by Autoclave, then pour the solution in sterile clean and dry Petri dishes, leave it to dry.

Result: colony Bacilli don't appear on filters, water samples were sterile, clean and free of the bacteria completely.

Table.2. Show the microbial results for the detection and enumeration of *E.coli* and coliforms of samples water

	permissible limits prescribe by Syrian S.N.S:45/2007 standards	Permissible limits prescribed by WHO standards	1	2	3	4	5	6
E.coli	0 / 100 ml	0 / 100 ml	-	-	-	-	-	-
Total Coliform	0 / 100 ml	0 / 100 ml	-	-	-	-	-	-

Figure.3. Show the microbial results for the detection and enumeration of *E.coli* and coliforms of some water samples

4. CONCLUSION

Results show that the values of water samples Nos. 1, 2, 3 don't match the specifications of water used in the pharmaceutical industry according to the Syrian standards and the United States Pharmacopeia. Sample No. 4 doesn't match the standards of calcium, sodium and nitrates. Sample No.5 doesn't match the standards of calcium and nitrates. Sample No.6 doesn't match the standards of sodium and nitrates.

One of the important tests to study the stability of drug is a chemical degradation reaction of active ingredient with metal ions. The presence of metal ions in the water used to solve dry powders leads to the interaction of the metal ions with the active substance and stimulates the interaction between the active substance and the excipients. In both cases, the production of unhealthy compounds and toxic complexions of the body (Saravanakumar, 2011; Blessy, 2014; Maninderjit Kaur, 2013).

In addition, a very important test for the study of the stability of the active substance of medicine is Oxidative test, it studies the drug degradation due to oxidized substances as chlorine. The presence of chlorine in water as a result of chlorination of water leads to oxidation and degradation of active substances in the suspensions and Produce harmful substances to the body (Saravanakumar, 2011).

The conditions for keeping the drug during consumption especially temperature stimulate the oxidation and degradation reactions between the mineral ions and the active substance. It leads to the production of toxic compounds for humans (Allen, 2012; Nishath Fathima, 2011).

Therefore, we don't recommend the use of water containing metal ions as ordinary tap water, cooled or boiled tap water or bottled spring water packaged in solving powder-based syrups.

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