**QUALITY CONTROL TESTS FOR SYRUPS & ELIXIRS**

**Syrups:** “Syrups are concentrated aqueous preparations of a sugar or sugar substance with or without flavoring agents and medicinal substances.”

Following tests are performed:-

1. Clean and purified vehicle (Distillation)
2. Light transmittance test
3. Visual inspection
4. pH measurement
5. Physical stability
6. Sucrose concentration (Assay of Active ingredient)
7. Refractive index
8. Specific gravity
9. Identification of Active ingredient
10. Optical rotation
11. Weight/ml (Density)
12. Viscosity
13. Alcohol determination (For Elixirs)

***1. Viscosity:***

“It is a property of liquid that is directly related to resistance to flow”.

Viscosity measurement is very important quality control test in case of syrups & elixirs.

Viscosity & consistency directly relates with stability of solutions.

**Types:-**

Viscosity is of following types;

**Absolute Viscosity:**

It measures when all specification & parameters are defined.

**Relative Viscosity:**

It measures when we take any standard & make comparison.

**Dynamic Viscosity:**

The resistance to flow encored when 1 layer or plane of fluid attempts to move over another identical layer or plane of fluid at a given speed. It is also called as absolute viscosity.

**Kinematic Viscosity:**

Addition & deletion of force is known as kinematic viscosity.

**Determination of Viscosity:**

Viscosity can be determined by following instruments;

**1.** Ostwald’s Viscometer

**2.** Falling Sphere Viscometer

**3.** Cone & Plate Viscometer

**4.** Cup & Bob Viscometer

**5.** Brook field Viscometer

Viscosity of syrup is determined by following apparatus;

 1. Falling sphere viscometer

 2. Rotational viscometer

i. Cup & Bob Viscometer

ii. Cone & Plate Viscometer

1. **Falling Sphere Viscometer**

**Principle:**

\* The principle of this instrument is based on stock’s law which state’s that “when a body falls through a viscous medium it experiences a resistance or viscous drag which opposes the motion of body”.

\* At initial state body experiences acceleration due to gravity but soon this acceleration is balanced by viscous drag & body falls with a uniform terminal velocity.

**Construction & working:**

\* It consist on a tube having 2 marking A & B on the outer surface.

\* The tube is filled with liquid whose viscosity is to be determined.

\* The tube is clamped vertically inside a constant temperature bath & significant time is allowed or equilibrium of temperature & removal of air bubble from the liquid.

\* A ball (glass-steel) is allowed to fall through tube.

\* Time taken by ball to fall from point A to B is noted & terminal velocity is calculated.

\* This is obtained by dividing distance between the 2 points with time.

1. **Rotational Viscometer**

It Works on the viscous drag in the body when it is retained in the fluid whose viscosity is to be determined, wide range of shear rate can be determined.

1. **Cup &Bob Viscometer:**

\* It consistsof 2 conical cylinder of different diameter.

\* The outer cylinder forms the cup into which the inner cylinder or bob is fixed centrally.

\* The sample to be analyzed is sheared in the space between the outer wall of the bob& the inner wall of the cup.

\* Torque setup in the bob is due to the rotation of the outer cup or due to rotation of bob itself (Searne type viscometer).

1. **Cone & Plate Viscometer:**

\* It consists of flat circular plate with a wide angle cone placed centrally above it.

\* During operation the sample is placed at the center of plate which is then raised into position under the cone.

\* The cone is driven by variable speed motor & sample is sheared in the narrow gap between stationary plate & rotational cone.

\* The rate of shear is rpm & is increased or decreased & torque produced is measured.

**Method**: Wash apparatus thoroughly with water. Then rinse with acetone and let it be air dried. Determine the density of water and assigned liquids with help of pycnometer. Fill the viscometer with water and suck up to upper mark A. Allow water to fall and record time of flow from mark A to B with the help of stop watch. Repeat the same procedure with all assigned liquids. Calculate viscosity by using formula;

**𝜂𝑙= (𝑡𝑙 × 𝑑𝑙) / (𝑡𝑤 × 𝑑𝑤) 𝜂𝑤**

**Application of Viscosity in Quality Control of Pharmaceutical:**

**Suspension & Creams:**

\* Viscosity is applicable in stability of suspension & creams.

\* Viscosity of medium plays an important role in stability of these products.

\* Viscosity of these products must be adjusted in such a way that gravitational pull must be counter balance by stability of these agents.

\* Suspending agent i.e. carboxymethly cellulose(CMC), tragacanth gum, hydroxypropyl methyl cellulose(HPMC) & xanthan gum must be use in preparation that will make active ingredient to be easy suspendible & the final product will be stable by enhancing the viscosity of the medium.

\* For example; metronidazole + flurazolidone suspension is prepared by using xanthan gum & CMC in 3:1 ratio for 1000kg. In a batch of 1000L xanthan gum can be used up to 3kg & CMC 1kg.

\* If the quantities of these agents are not sufficient then viscosity of the suspension is less & caking will develop.

**Ointment:**

It is composed of oil based medium i.e. soft & hard liquid paraffin. By increasing or decreasing the quantities of these ingredients viscosity is brought to decreased level.

**Suppositories:**

\* The viscosity of melted mass of suppositories is important in their manufacturing &their behavior in the rectum; some of these suppositories have less viscosity whereas propylene glycol type of suppositories has good viscosities.

\* In the manufacturing of suppositories with low viscosity bases extra care must be exercised to avoid sedimentation of active ingredient this cause uneven distribution of active ingredient to prevent the segregation of the particles & the molten bases, the molten bases are handled at lower temperature & solidified quickly in mold.

\* To overcome such a problem the base having melting point near body temperature is use.

\* 2% of aluminum monostearate increases the viscosity of the base & also help to maintain homogeneous suspension of insoluble material.

**Soft gelatin capsule:**

\* The capsule shell is composed of gelatin, plasticizers % water.

\* Physico-chemical properties of gelatin make it an ideal substance for the capsulation of pharmaceutical products.

\* The viscosity of gelatin can ranges from 25-45cp of the production of gelatin product.

\* However most of the gelatin manufacturers set the gelatin viscosity up to 40cp.

\* For the capsulation of hygroscopic material viscosity of gelatin must be 25-30cp.

**Role of viscosity in syrups:**

\* Viscosity plays a major role in manufacturing of syrups.

\* E.g. if the viscosity of syrup is low it will cause difficulty during filling the syrups in bottles. Some of the syrup is flow out of the bottle when it is filled with pressure.

\* To overcome this problem the viscosity of syrup will increase by adding small quantities of CMC, HPMC or HPC.

\* Similarly if the viscosity of syrup is too high patient will feel difficulty while pouring the syrup out of the bottle therefore viscosity of syrup is maintain in considerable range.

**Role of viscosity in tablets:**

In tablet manufacturing viscosity play an important role as tablet binder & retard the release of drug from matrix (extended release tablets). E.g. HPMC, PVP & Ethyl cellulose.

***2. Clean& purified vehicle (water):***

The water is filtered & purified at the plant to destroy any microorganism & to remove particles from the water.Quality control technicians test the water frequently to ensure that it is clean & pure before the syrups & elixirs made.The syrups & elixirs are also thoroughly filtered before filling in bottles.

***3. Light Transmittance Meter:***

A light transmittance meter is a tool i.e. used to check the syrup’s color.In a light transmittance meter a syrup sample is check for color by passing the light to the sample.The %age of light transmittance is compared to light transmittance rates set for different grades.When using one, you should be sure that there is no finger prints on syrup test bottle, and that the syrup sample has no bubbles or cloudiness.Any of these conditions may diminish the light i.e. transmitted through the sample & therefore lower the grades of sample.

***4. Visual inspection:***

With the visual inspection, the ingredient & the final product are carefully examined for purity&for appearance. Physical appearance of product for patient adherence &compliance is critical so that it should be good looking & elegance in appearance.

***5. pH measurement:***

The measurement & maintenance of pH is very important step in quality control testing.Generally there are 2 different types of methods use in the measurement of pH;

**Methods for pH measurement:**

1. **pH paper:**The simplest & cheapest method is to dip a piece of pH paper into the sample.The sample is impregnated with chemicals that change the color & color may be compare to a chart supplied with the paper to give the pH of the sample.
2. **pH meter:**If greater accuracy is required a pH meter should be use.A typical pH meter consist of special measuring glass electrode connected to an electronic meter that measures & display the pH reading.

***6. Physical Stability of Syrups:***

* The syrups must be stable physically e.g.
* Its appearance (no crystallization and microbial growth)
* Color must be completely soluble with other ingredients.
* Odor and taste (palatable)
* Solid material is completely miscible in liquid.

***7. Sucrose concentration/Assay of active ingredient:***

The determination of sucrose concentration is also very important in quality control testing of syrups.If the concentration of sucrose in the syrup is very high it may crystallize the syrup & less concentration give favor for the microbial growth.There is no specific method for the determination of sucrose in syrup we use **HPLC & U.V spectroscopy** for this purpose.

1. **By using HPLC**

HPLC technique is used for both qualitative & quantitative analysis of sucrose.For qualitative analysis or to confirm the presence of sucrose we compare the peaks obtained after running HPLC with standards & specific peaks of sucrose. For quantitative analysis we measure the area under curve (AUC) that will tell us about the concentration of sucrose present in given sample.

1. **By using U.V spectrophotometer**

It can be used for quantitative analysis, by using Beer’s lambert law.The concentration of single absorbing species in a solution can be readily determined.The absorptivity’s of many substances at specified wavelength are available in literature.However, if any absorbance is not available it can be determined by measuring the absorbance of a solution of known concentration of the substance concerned, using Beer’s lamberts law.

**Specification:**

* B.P = 66.7 % w/w
* USP = 85 % w/v

***8. Weight/ml (Density):***

1.315 to 1.333 g

The weight per milliliter of a liquid is the weight in g of 1 ml of a liquid when weighed in air at 20°, unless otherwise specified in the monograph.

**Method:** The weight per milliliteris determined by dividing the weight in air, expressed in g, of the quantity of liquid that fills a pycnometer at the specified temperature by the capacity, expressed in ml, of the pycnometer at the same temperature. The capacity of the pycnometer is ascertained from the weight in air, expressed in g, of the quantity of *water* required to fill the pycnometer at that temperature. The weight of a liter of *water* at specified temperatures when weighed against brass weights in air of density 0.0012 g per ml is given in the following table. Ordinary deviations in the density of air from the above value, here taken as the mean, do not affect the result of a determination in the significant figures prescribed for Pharmacopeial substances.

**Temperature (°C)** **Weight of a liter of water (g)**

20 997.18

25 996.02

30 994.62

**Density:** The density, of a substance is the ratio of its mass to its volume at 20°. It is expressed in kg m-3.The densityis determined by dividing the weight in air of the quantity of the liquid being examinedthat fills a pycnometer at 20° by the weight in air of waterrequired to fill the pycnometer aftermaking allowance for the thrust of the air.

The densityis calculated from the expression

Where M1 = weight in air (apparent mass) in grams of the substance being examined,

 M2 = weight in air (apparent mass) in grams of water,

 A = the correction factor for the thrust of the air, 0.0012M2,

 998.2 = the density of water at 20° in kg m-3.

In most cases, the correction for the thrust of the air may be disregarded.

***9. General appearance:*** Clear concentrated aqueous solution

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***10. Clarity:*** Clean & clear with no solid particles.

***11. Determination of alcohol concentration (only for elixirs):***

Elixir usually contains 5-40% alcohol. The determination of alcohol unless otherwise specified in the individual monograph.It is suitable for examining most fluid extract & tinctures & elixirs provided the capacity of distillating flask is sufficient (size of distillating flask should be 3-4times larger than the volume of sample used) & the rate of distillation is such that clear distillates are produced.Cloudy distillates may be clarified by agitation with talc or with calcium carbonate & filtration is done.After which the temperature of filtrate is adjusted & the alcohol content is determined from the specific gravity.During all manipulation, take precaution to minimize the loss of alcohol by evaporation.

***12. Refractive Index:***

It is measured by **refractometer.** Refractive index **= 1.4608 - 1.4630.**

**Method:** Place the apparatus in front of proper light source.Clean the apparatus using soft cloth and wipe the prism by soft brush, if necessary, moistened with alcohol and then acetone.Place a drop of distilled water and adjust the instrument.Focus the telescope eye piece on the cross section of the instrument and rotate the index arm until a colored band or fringe is seemed through the telescope.Adjust the eye piece on the movable arm to give sharp focus on the scale and record the refractive index to the third place of decimal and for fourth place use a reading lens. Take at least three readings of each sample and its mean used for calculation.Open the prism by turning the lock nut and clean the face of the prism. Put a few drop test solution on prism and close it properly.Take three readings of each sample of liquid

***13. Identification of active ingredient:***

Identify active ingredient by test like 1g of invert syrup + 5ml of potassium cupric tartrate, give rise to formation of red precipitate.

***14. Solubility:*** Syrup should be soluble in water.

***15. Optical rotation:***

Range is **50°-60°**. Syrup should not be less than **50°** & not more than **60°**. It is to check the **inversion of syrup**.

**Method:** A simple polarimeter was built by using a light bulb, color filters, polarizing filters, and a sample cell. Then prepared 100 - 200mm long columns of water solutions of sugars (sucrose, fructose, dextrose, and lactose). Then measured the optical rotation of the sugars in solution by rotating the analyzer in the polarimeter until no light was transmitted.

***16. Specific gravity:***

Specific gravity of syrup either 66.7% w/w or 85% w/v should be **1.313.**

**Method:**

Wash pycnometer thoroughly with water. Then rinse with acetone and let it be air dried. Weigh the empty pycnometer with stopper. Fill the pycnometer with water and weigh it. Subtract weigh of empty pycnometer from this reading to find the weight of water. Now fill the pycnometer with all assigned liquids one by one and weigh. Subtract weigh of empty pycnometer from reading to find the weight of each liquid. Determine the specific gravity of each liquid by using formula:

**𝑠𝑝𝑒𝑐𝑖𝑓𝑖𝑐 𝑔𝑟𝑎𝑣𝑖𝑡𝑦= (𝑤𝑒𝑖𝑔ℎ𝑡 𝑜𝑓 𝑠𝑢𝑏𝑠𝑡𝑎𝑛𝑐𝑒)/(𝑤𝑒𝑖𝑔ℎ𝑡 𝑜𝑓 𝑒𝑞𝑢𝑎𝑙 𝑣𝑜𝑙𝑢𝑚𝑒 𝑜𝑓 𝑤𝑎𝑡𝑒𝑟)**