Official solutions prepared by simple solution with sterilization

Ophthalmic Solutions

Sterile solutions that are applied to the eye either for local effect or for treatment of interior parts of the eye

should be

isotonic, buffered to pH 7.4, viscous, and properly packaged

Volume

Small volume as eye drops

or

Large volume as cleaning solution or for contact lenses

Some instruction for uses of ophthalmic solutions

1. Because the capacity of the eye to retain liquid and semisolid preparations is limited (5-10 µl), topical application are administered in small amounts. Not more than one drop is put in the eye.

- If we have multiple drop therapy, there should be at least 10 min between the applications of each type.

2. Patient should not touch the tip of the dropper with the infected eye tissue.

Requirement of ophthalmic solutions

1. Sterility and presence of anti-microbial agent (or preservatives) all ophthalmic solutions or most should be sterilized using auto-clave at 121°C for 15 min except those which are unstable at the auto-clave condition, they sterilized by another method such as by using micro-filter, which is a physical membrane that has pore size that prevent bacteria and foreign materials from passage into ophthalmic solution. However, this method is not efficient as auto-clave method.

- Other methods such as using of gases and rays can also be used.

- Ophthalmic solutions should be prepare in aseptic area, so all utensils and personnel should be clean and sterile, also the room are specially designing, so that the corner of the wall should be curvature and also there is a hood pushing sterile stream of air so push all bacteria and foreign bodies outside of the room.
- In addition to sterility, the ophthalmic solutions of multi-dose type should contain preservative, so that the microorganism introduced to solution accidently will show no growth.
- For ophthalmic solution used for surgical operation or for traumatized eye there is no need for preservative because:

1. They are single dose product.
2. The preservative be irritants for open eye tissue.

The properties of the preservatives used in ophthalmic solutions

1. Should be effective at the used concentration.
2. Should be inert do not interact with active ingredient or container material.
3. Stable
4. Should not adsorb to the wall of the container.

Examples of preservative used in ophthalmic solutions:

1. Benzylkonium chloride which is used in concentration between 0.004-0.01% w/v. It is quaternary ammonium compound, it acts as preservative by ion exchange with carboxyl group of cell wall of microorganism and it cause lyses of microorganism. It should not be used for anionic compound because it neutralized and its activity will impair.

2. Chlorbutanol is used in concentration 0.25-0.5% w/v. it is hydrolyzed and decomposed at auto clave temperature, also it is hydrolyzed slowly at moderate and at room temperature with production of hydrochloric acid.

- So this hydrolysis and degradation is not only render a product susceptible to microbial growth but also could alter its pH and thereby affect the stability and/or physiologic activity of the drug.
- Efficient buffer should be used to prevent change in the pH of the product.

3. Thiomersol used in concentration 0.001-0.5% w/v.

4. Methyl/propyl parabens used in concentration 0.05-0.01% w/v: mixture designed to exert antibacterial and antifungal effects.

- Generally ophthalmic solutions are sterilized by auto clave at 125^{o}C for 15 min but certain drugs are thermo-stable in acidic media at auto clave temperature and become thermo-labile (sensitive to heat) at pH 7.4 at auto-clave temperature.
- So in such case we sterilize the product by auto clave in acidic media then we add buffer to change the pH to 7.4 (physiologic pH).
- The addition of buffer should be in aseptic area.

Isotonicity

- Ophthalmic solution should be isotonic with lachrymal fluid.
- Isotonic mean equal tone; if the ophthalmic solution is hypertonic so when applied to eye the solvent will get out of the cell, so we have shrinkage of eye tissue, and if the ophthalmic solution is hypotonic, so swelling occur to the tissue.
- In both cases discomfort feeling will result, for this reason tonicity should be adjusted. Eye can tolerate practically a tonicity 0.6-2% without marked discomfort to the eye. Sodium chloride itself does not have to be used to make the solution isotonic but boric acid in a concentration of 1.9% is used to produce the same osmotic pressure as does 0.9% sodium chloride.

Buffering

- Buffering of ophthalmic solutions means adjustment of ophthalmic solution pH close to lachrymal fluid pH 7.4 as much as possible. The benefits of buffering ophthalmic solutions are:

A. To reduce discomfort to the patient: the patient feels discomfort if ophthalmic solution pH is too high or too low, but after a short time he will fell comfort because the buffer capacity of tears get rid of excess H^+ ions or OH^- ions, but there are some drugs that are quite acidic that will overcome the buffer capacity of tears. Example of such drugs pilocarpine HCl and Epinephrine bitartarate.

B. To control stability: some drugs are unstableat the lachrymal fluid pH so another pH medium should be chosen.

C. To control therapeutic activity: if we want to treat the interior part of the eyes, then the drugs must be unionized to cross lipid membrane of the eye and this depend on pH. So we should select the pH that part of the drug will be ionized and part of it will be unionized; that a good thing for therapeutic activity and good for solubility. Solubility of alkaloidal salt is decreased at the pH level of lachrymal fluid pH and precipitates. So to adjust pH, a suitable pH buffer must be used.

USP described two buffers for ophthalmic solutions these are:

1. Boric acid buffer that provide pH slightly below 5, this buffer is suitable for many soluble salts of cocaine, phenylephrine, pilocarpine and tetracaine.
2. Phosphate buffer that provide a pH 5.9-8.0, it is suitable for many drugs except salt of pilocarpine, homatropine because they are unstable in this buffer.

Viscosity

- Ophthalmic solutions should be viscous enough, so the drug will be in contact with eye tissue for a long period of time and prevent drainage of ophthalmic solutions.
- So a suitable viscosity increasing agent is used as 1% methyl cellulose, which gives viscosity 25 cps. This substance is also used as tear replacement. The optimal viscosity for ophthalmic solution is between 15 to 25 cps.

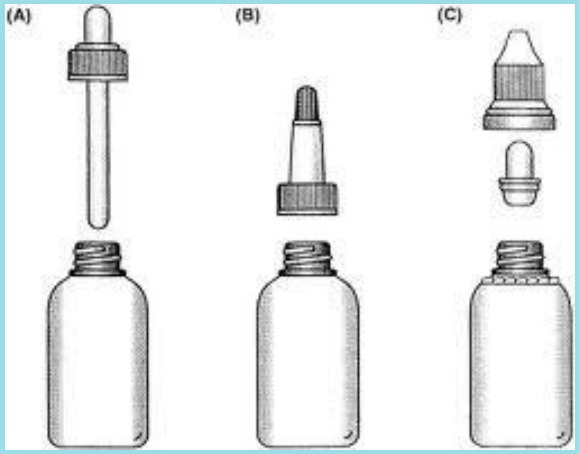
Proper packaging

- The important thing is the product should be packed in a container so the solution is easily administrated, active constituents are stable and the sterility is maintained. We have two type of containers:

1. Glass containers
2. Plastic containers

- The disadvantage of glass containers is that the alkaline substance is leached from the glass container to ophthalmic solution causing an increase in the pH of the solution.
- The disadvantage of the plastic container is the interaction of the substance of the container with the preservative used or it allow separation of some medicinal agents.
- The dropper of ophthalmic solution is either fixed dropper or screw dropper. Fixed dropper is better because there is a low chance for microorganism to be introduced into the solution. The solvent used should be sterile distilled water or water foe injection.

Fixed and screw dropper



Contact lenses solutions

- Contact lenses may be hard, soft or rigid gas permeable (RGP).
- Solution which are used for taking care of contact lenses are used as wetting solutions, cleaning solutions, soaking solutions or combined purpose solutions.
- It is very important to take care of contact lenses, if we do not take care of them then infection will takes place and if it occurs this may result in blindness, also if the lenses are not clean then it modify the sight.