

INDUSTRIAL PHARMACY-I

UNIT IV-PARENTERALS

CLASS:33

TOPIC Ophthalmic Preparations: Introduction, formulation considerations; formulation of eye drops

- Ophthalmic products are the sterile products meant to instillation in to the eye in the space between eye lid and the eye ball.
- Three ways can do the instillation of the specialised dosage forms into the eyes:
 - 1) topical (onto the external surface of the eye), 2) intraocular (administered inside) and
 - 3) periocular (adjacent to the eye). Sometimes these formulations are also used in conjunction with an ophthalmic device.
- These are known as ophthalmic dosage forms

Types of ophthalmic products

- Ophthalmic products may be categorized into a number of groups:
- **Liquid preparations** for application to the surface of the eye such as eye drops and eye lotions.
- **Semi solid preparations** such as eye ointments, creams and gels for application to the margin of eye lid or for introduction in to the conjunctival sac.
- **Solid preparations** such as Ocular inserts intended to be placed in contact with the surface of the eye to produce modified release of medicament over a prolonged period.
- **Parenteral products** for sub conjunctival or intra ocular injection
- **Liquid products** for irrigation of the eye during surgical procedures.

All ophthalmic products are required to be sterile and free from extraneous particulate matter. Solutions used during surgery should not contain any preservative

REQUIREMENTS

- Ophthalmic preparations should possess the following properties:

- Foreign particles
- Viscosity
- Tonicity
- pH of preparations
- Sterility
- Surface activity

Foreign particles

- All the ophthalmic products should be clear and free from foreign particles, fibers and filaments.
- Ophthalmic solutions should be clarified very carefully by passing through bacteria proof filters such as membrane filters, sintered glass filters.
- The particle size of the eye suspension should be in an ultrafine state of subdivision to minimize irritation.
- A separate filter should be used for different ophthalmic products in order to avoid the contamination.

Viscosity

- Optimum viscosity is an essential character for any ophthalmic formulation which prolongs the contact time of the drug in the eye.
- To achieve the desired viscosity, add one or more thickening agent in the ophthalmic preparations.
- Some of the commonly used viscosity enhancers are
 - polyvinyl alcohol (1-4%),
 - polyethylene glycol,
 - methylcellulose,
 - carboxymethylcellulose.
- Desired properties an ideal thickening agent:

1) Easy to filter.

- 2) Easy to sterilize.
- 3) Compatible with other ingredients.
- 4) Must have requisite refractive index and clarity level.

Due to some possible adverse effects, in the formulation of eye drops and eye lotions which are required to be used during or after surgery on the interior of the eye, thickening agents are not included

Tonicity

- Isotonicity with lachrymal secretions is very much desirable in all the ophthalmic products to avoid discomfort and irritation.
- On average, an eye can only tolerate a range of tonicity equivalent to 0.5-2% solution of NaCl.
- To adjust tonicity, prepare ophthalmic products with certain isotonic vehicles such as 1.9% boric acid, sodium acid phosphate buffer.

The pH

- the pH has a vital role in the therapeutic activity, solubility, stability and comfort to the patient.
- Tears have a pH of about 7.4.
- An eye can tolerate solutions of wide pH range as eyes have its control system for pH.
- Alkaloid salt solutions are stable at pH 2-3 pH, which is irritant to eye.
- The alkaloids get precipitated at pH above 7 and create several formulation problems.
- Benzalkonium chloride, polysorbate 20, polysorbate 80, dioctyl sodium succinate are some of the surfactants which are commonly used.

Sterility

- Ophthalmic preparations must be sterile when prepared.
- Pseudomonas aeruginosa is very common gram -ve bacteria which is generally found to be present in ophthalmic products.
- It may cause serious infections of cornea. It can cause complete loss of eye sight in 24-48 hrs.

- To maintain sterility in multi dose container, containing ophthalmic products, a suitable preservative is added. The preservative should be non-toxic, non-irritant and should be compatible with medicaments.
- The ophthalmic products are generally sterilized by autoclaving, filtration through bacteria proof filters and addition of bactericides at low temperature.

Surface activity

- Vehicles used in ophthalmic preparations must have good wetting ability to penetrate cornea and other tissues.
- Certain surfactants or wetting agents added which are found suitable for ophthalmic products.
- It should not cause any damage to the tissue of eye.
- Benzalkonium chloride, polysorbate 20, polysoabate 80, dioctyl sodium sulpho succinate etc., are some of the surfactants which are commonly used.

EYE DROPS

- Eye drops are sterile aqueous or suspensions of drug that are instilled in to the eye with a dropper.
- They usually contain drugs having anti septic, anti anesthetic, anti inflammatory, mydriatic or meiotic propertie

FORMULATION

- Drug
- Preservative
- Sterilization
- Isotonicity
- Buffer
- Viscosity
- Container
- label

Drug

- These contains drug of various categories including antiseptic, anti-inflammatory agent, mydriatic or meiotic properties.

Preservative

- Eye drop should be sterile and should contain preservatives to avoid microbial contamination when the container is open.
- The preservative for ophthalmic use includes Benzalkonium chloride, Chlorbutanol, Phenylmercuric acetate, Phenylmercuric nitrate etc

Isotonicity

- All the solutes including drug contribute to the osmotic pressure of the eye drop, therefore isotonicity of the formula should be calculated and it is adjusted with sodium chloride, for example- Sodium chloride 0.9% and boric acid 1.9% are iso-osmotic.

Buffer

- The buffer should be added to maintain balance between comfort, solubility, stability and activity of drug.
- For example-, the hydrolyzed chlorbutanol forms hydrochloride acid making the drop acidic, whereas certain drug like pilocarpine hydrochloride are acidic.
- On the hand certain drug such as alkaloids show precipitation at lachrymal pH.
- Boric acid, monobasic sodium phosphate are the common buffers for eye drop

Viscosity

- The size of drop and its residences in eye depends on viscosity of eye drops.

Methylcellulose, hydroxypropyl methylcellulose and polyvinyl alcohol are common viscosity enhancer

Container-eye drops

- The commonly used container for ophthalmic solutions or suspension is multi-dose container (5ml, 10ml).
- Glass container is supplied with sterile plastic dropper.
- Plastic bottles are with built-up nozzle

Label

- Not for injection.
- For external use only.
- Shake well before use (if it is suspension)

PREPARATION

- The eye drops are prepared in 4 stages.
 - Preparation of the solution
 - Clarification of the solution
 - Filling into the container
 - Sterilization of the formulation
- The aqueous vehicle may support bacterial or fungal growth,
 - so one of the following bactericide may be used to prepare the eye drops :
 - Phenyl mercuric nitrate/ acetate – 0.002%
 - Benzalkonium chloride – 0.01%
 - Chlorhexidine acetate-0.01%

Preparation of solution of medicaments and adjuvant:

- The medicaments are dissolved in the aqueous vehicle containing suitable anti microbial agent.
- Phenyl mercuric nitrate/ acetate 0.002%
- II. Benzalkonium chloride 0.01%
- III. Chlorhexidine acetate-0.01%
- The adjuvants are also dissolved in the vehicle at a stage to form a stable preparation.

Clarification:The eye drops are clarified by passing the solutions through membrane filter having pore size of 0.8 μ m.

- The clarified solution is immediately transferred in to final containers and sealed to exclude micro organisms.

Sterilization : the eye drops are sterilized by autoclaving or heating with bactericide at 98° to 100°C for 30 mins., or filtration through bacteria proof filter.

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