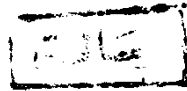


AN IDEAL EYE DROP IN OPHTHALMIC PRACTICE

THESIS

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HISTORICAL BACK GROUND



INTRODUCTION

INTRODUCTION

The eye drops or collyria "single collyrium" can be defined as sterile solutions that are compounded and packaged for instillation into the eye. It must include the phrase free from foreign particles. Collyria should be non-irritant, should be sterile, should be clear, should not inhibit the action of tear lysozyme and should be contained in sterile containers (USP XIX 1975).

Duck -Elder, in 1962, said that eye drops should be non irritant and this depends on the temperature, the reaction and osmolarity of these drops.

The temperature of eye drops should be that of the body, but this requirement is more important when we use eye lotions which should be warmed by dilution with warm water but in case of eye drops where they are contained in small sized containers, this requirement is unnecessary.

The reaction is most important factor determining the irritability of collyrium. This reaction depends mainly on hydrogen ions concentration rather than the osmotic pressure (tonicity) or the drugs present in the ophthalmic solutions.

Immediate discomfort which occurs in the eye following instillation of an eye drop is due to the fact that its PH is different from that of tears which is approximately 7.4 but may vary between 6.6 and 9.0. This is why the reaction of the collyrium should be near that of tears. To overcome this problem, a properly formulated eye drop must contain a buffer system with a capacity adequate for stability and to allow the tear fluid to readjust the PH to 7.4 after instillation and prevent more discomfort to the eye.

Several considerations must be taken during the use of eye drops in order to prevent contamination. On instillation great care must be taken to prevent touch of the dropper or bottle tip to the lids or the lashes and if it occurs it must be discarded in cases of highly infected eyes and when blepharospasm is so severe that touch of the lids can not be prevented. In these circumstances the droppers must be used once and then resterilized or discarded and we use disposable plastic droppers. One bottle must be used for each patient and then discarded after 2-3 weeks from use.

In multidose containers which are used more than once, a bactericidal preservative or a mixture of preservatives must be contained in sufficient concentration to prevent the growth of micro-organisms accidentally introduced into the container during the use of eye drops. An ideal eye drop should not inhibit the action of lysozyme naturally present in tears which has bacteriostatic activity (Duke-elder 1962).

Ridley, in 1948, studied the effect of different medicaments on the activity of lysozymes. He found that the free halogen group such as eusol destroy lysozyme even in high dilutions. Silver nitrate and copper sulphate destroy it up to very high dilution. The other drugs tested such as, zinc sulphate, argyrol, boric, mydriatics, myotics, cocaine have no bad effect on lysozyme.

Roehrs, in 1982, said that an ideal eye drop must be clear from any foreign particles. This can be achieved by filtration of eye drops during manufacture. Also to be ideal for ophthalmic use there are several physiological properties which determine the absorption of active ingredients,

the comfort and the stability of eye drops :-

1- Viscosity of eye drops and the viscosity imparting agents which increases the contact time between the eye drop and the eye increasing its bioavailability.

2- The hydrogen ion concentration "PH" and buffer system used which has great influence on drug absorption, comfort of eye drops, and stability of eye drops.

3- Tonicity and tonicity adjusting agent which has an effect on the comfort of eye drops and control the therapeutic drug concentrations.

4- Lipid solubility of active ingredients to penetrate the cornea.

Also, in 1982, Roehrs and others stated some dosage forms of eye drops :-

a- Solutions :- (See fig. 1, p.5 "A")

Nearly all of the major ophthalmic therapeutic agents are water soluble or can be formulated as water-soluble salts. A homogeneous solution has the advantages of greater assurance of uniformity of dosage and bioavailability and simplifies the large scale manufacture.

b- Suspensions:- (See fig. 2, p. 5 "A")

If the drug is not sufficiently soluble, it can be formulated as suspension, also suspension may be desired to increase stability, bioavailability and efficacy. For example water-soluble salts of prednisolone phosphate are available but they have a lower steroid potency and are poorly absorbed. The major topical ophthalmic suspensions are the steroids.

c- Powders for reconstitution :- (See fig. 3, p. 5 "B")

Many ophthalmic drugs are prepared as sterile powders for reconstitution by the pharmacist before dispensing to the patient. Examples are chloramphenicol and epinephrine.

The sterile powder is obtained by lyophilization and is packaged separately



Fig.1 : Dosage forms of eye drops : Solutions. From the Wellcome Foundation Ltd London.

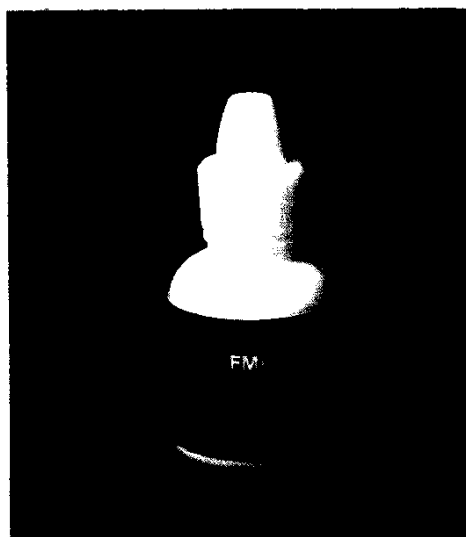


Fig.2 : Dosage forms of eye drops : Suspensions. From Allergan International Company California, U.S.A.

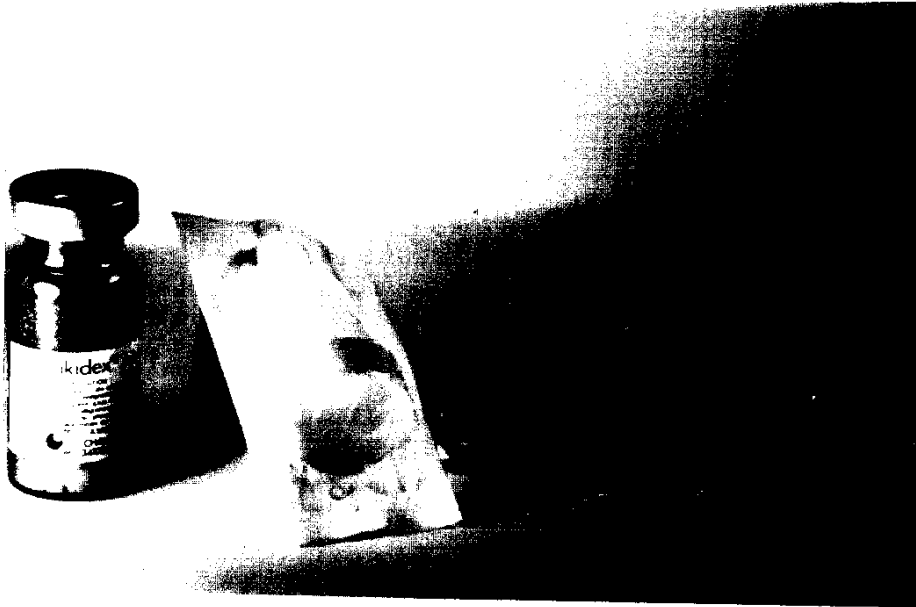


Fig.3 : Dosage forms of eye drops : Powders for reconstitution. From Laboratories of Chauvin-Blache, *France*.

from the diluent which has a preservative and a sterile dropper is provided separately. In this powder form these drugs have longer shelflife than that of solution forms.

" ADMINISTRATION OF EYE DROPS "

Before use of eye drops one should wash his hands. The usual method for self-administration of eye drops is to place the eye drop from a dropper or dropper bottle into the lower cul-de-sac by pulling down the eyelid, tilting the head backwards, looking up at the ceiling while the tip is pointed close to the sac but without touching anything and applying a slight pressure to the rubber bulb or plastic bottle to allow a single drop to form and fall into the eye. Meantime a finger should compress the lacrimal passages at the inner canthus to minimize the drainage, then release lower lid, the eye must be closed at least for 30 seconds and light massage of the lids is done to distribute the medicament over the globe. This manoeuvre is difficult for the elderly, arthritic, low vision and glaucoma patient and may require another person to instill the drops (Roehrs et al 1982). (See fig. 4, p. 6 "A")

Ahmad Mansour et al, in 1984, used a spray bottle to deliver topical ophthalmic solutions instead of the classic dropper delivery system for use in arthritic patients and in pediatric age group. It can be used in any position including one lying prone after retinal surgery and to deliver topical anaesthesia for tonometry, while the patient is seated at the slit lamp. (See fig. 5, p. 6 "B")



Fig.4 : The usual method for self-administration of eye drops described by Roehrs, R.E. , Hecht G. and Shively , C.D. : Design and evaluation of ophthalmic pharmaceutical products. In Banker, G.S. and Rhodes, C.T. (editors): Modern pharmaceuticals, pp. 479-510, 1982. Marcel Dekker inc.

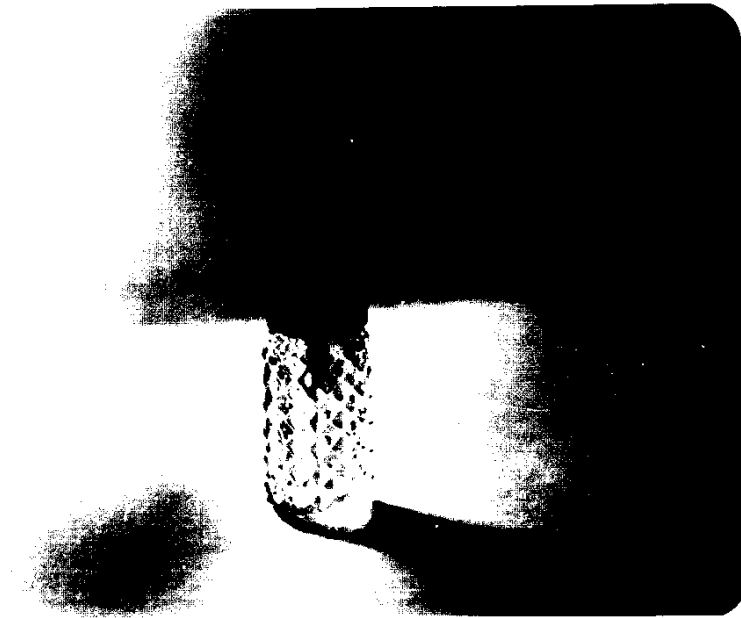


Fig 5 : Spray bottle to deliver topical ophthalmic solutions described
by Ahmad Mansour et al (1984) , Am. J. Ophthalmol. 97 (2) : 245, 1984.

Fraunfelder, in 1976, has reported a modification which results in "depo" application effect. It consists of pulling the lid away from the globe and applying the drop to the formed potential pouch.

After waiting a moment to allow the drop to gravitate to the base of the cul-de-sac and then lift the lid upward to touch the globe and thereby trap some of the solution in the lower conjunctival sac. By using a radioactive tracer, he found that this manoeuvre increased significantly the corneal and ocular retention time.

There is no special eye drops with specific doses for pediatric use as in other oral, parenteral, nasal and suppository dosage forms. But certain eye drops which contain medicaments with systemic toxic effects as atropine must be used with great care in children and their frequency of use must be much minimized. Several doctors reported toxicity from atropine and hyoscine eye drops in children.

The administration of eye drops to young children is a difficult method. A manoeuvre was described where parent sits on the floor or flat surface and placing the child's head firmly between the parent's thighs while crossing legs over the child's lower trunk and legs. The parent's hands are then free to instil the eye drop in the lower conjunctival sac.

(Roehrs et al 1982)

" FREQUENCY OF USE OF EYE DROPS "

It was found that the frequency varies greatly according to the type of the drug used and the disease. For example, in case of timolol eye drops which is a beta-blocker used for glaucoma, it is preferred to use twice daily