

A REVIEW ON EYE DROP**Devyani S. Watmode, Pooja R. Hatwar*, Dr. R. L. Bakal and Mayuri V. Rom**

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Maharashtra, India.**ABSTRACT**

Eye drops are liquid drops applied directly to the surface of the eye usually in small amounts such as a single drop or a few drops. When using eye drops, even when used correctly, there may be multiple routes of absorption, and if the eye drops are not fully absorbed by the eye, an overdose can sometimes lead to poor systemic bioavailability. Eye medication for anterior chamber disorder is delivered through eye drops or through a slow-release device inserted into the eye into the tear fluid. The instilled drug exits the eye in several ways, including through the canaliculus, which drains tears into the nasal cavity and is transported through the various eye membranes. A disease that affects the ocular surface, it is important to understand how repeated use of eye drops affects the ocular surface, affects clinical signs, affects symptoms, and affects the overall dry eye process. The ingredients in topical formulations most likely to adversely affect the ocular surface are preservatives.

KEYWORD: Eye drop, ophthalmic preparation, Corticosteroids, Sympathomimetics.**INTRODUCTION**

Delivering drugs to the human eye is an important part of medical care. Ophthalmic drug delivery is one of the most interesting and challenging jobs for pharmaceutical scientists. Due to the anatomy, physiology and biochemistry of the eye, this organ is extremely insensitive to foreign bodies. A major challenge for formulators is bypassing the eye's protective barrier without causing permanent tissue damage. Newer, more sensitive diagnostic techniques and the development of novel therapeutic agents continue to provide ocular delivery systems with high therapeutic efficacy.^[3] The stratified, nonkeratinized squamous cells that make up the cornea and conjunctiva's epithelium secrete mucins, which are glycosylated glycoproteins.

Mucins are crucial for maintaining the integrity of the tear film because they create the glycocalyx, which lubricates the mucosal barrier and helps the aqueous layer cling to the hydrophobic cornea. Goblet cells, specialised epithelial cells, are scattered throughout the conjunctival epithelia. These are the only cells that release the gel-forming mucin MUC5AC, which is vital for protecting and preventing desiccation of the ocular surface. Therefore, morphological alterations, goblet cell loss, or changes in their function negatively affect the tear film and ocular surface.^[4]

The simplest and least invasive method of delivering medications to the eye's anterior region is topical administration. Therefore, eye drops which account for 90% of the commercialised items in the worldwide ophthalmic medicine market are the preferred treatment for many ocular illnesses such infection, inflammation, glaucoma, dry eye, and allergies. However, topical administration's principal drawback continues to be its very poor efficacy. Due to the specific physiology and structure of the eye, drug distribution through the anterior segment is restricted and has low bioavailability.^[2]

Their clinical usefulness may be hampered by multiple daily injections and local eye discomfort. Clinical efficacy of aqueous eye drop formulations can be increased by increasing their topical absorption and decreasing eye discomfort. Previous research demonstrated that the delivery of dorzolamide and closely related CAIs into the eye is enhanced by eye drop solutions that are acidic as opposed to neutral.^[4]

Given monacaprins limited solubility in water, eye drops are sterile liquid dosage forms that may not be appropriate monacaprins carriers. However, the inclusion of excipients can enhance solubility. Additionally, viscosity enhancers, such as carboxymethylcellulose (CMC, E number E466) and (Hydroxypropyl)methyl cellulose (HPMC, E number E464), which are both long chain polymers derived from cellulose and frequently used in food and pharmaceutical products, can be added to eye drops to lengthen the time they are retained on the eye. Both CMC and HPMC, ocular viscosity-enhancing polymers with good safety histories, are frequently employed in ophthalmic preparations.^[5]

Due to its properties for drug disposition, the eye is the most fascinating organ. Any drug molecule taken via the ocular route must first penetrate the precorneal barriers to reach the anatomical barrier of the cornea, which is why topical administration is typically favoured for eye conditions over systemic administration. The tear film and conjunctiva are the first

barriers that prevent an active substance from entering the eye quickly. When administered, the medication stimulates the physiological mechanisms that act as a protective barrier against ophthalmic drug delivery, such as tear production.^[6] Direct application of the ocular formulation on the surface of the eye is the method used most frequently to provide medications to the eyes. The most popular formulation for anterior segment diseases is eye drops, however they are quickly removed by tears within 0.5–1 minute after application. As a result, a drug's action on the ocular surface lasts just a brief time.^[7]

Pharmaceuticals that are injected into the eyes, such as eye drops and ophthalmic medicines, are used to treat and prevent a variety of ocular illnesses. One of the primary sensory organs of the living world are the eyes. An essential component of medical care is the administration of drugs to the human eye. One of the most intriguing and difficult tasks facing pharmaceutical scientists is ocular medication delivery. The eye's architecture, physiology, and biochemistry make it extremely resistant to outside materials. The formulator faces a huge hurdle in getting through the eye's protective barriers without enduring long-term tissue damage.^[8]

Advantages^[3]

The advantages of ophthalmic solutions include

- a. Low cost and simple manufacture compared to alternative dose designs.
- b. The dose uniformity of ophthalmic solutions may be enhanced.
- c. Increased ocular bioavailability.

Quality^[3]

Ophthalmic solution must

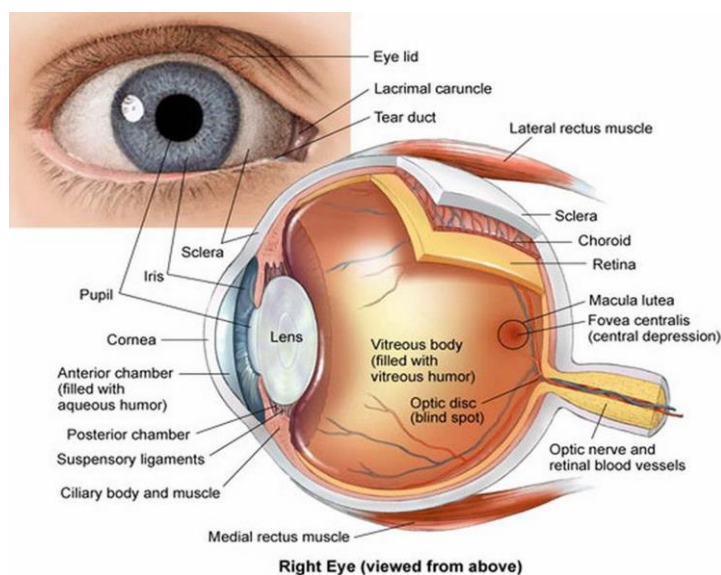
- a. Increase the proportion of local to systemic effects.
- b. Be simple to administrate yourself.
- c. Does not leave a particularly terrible aftertaste, persistent blurring, or a feeling of a foreign body.
- d. Be capable of industrial-scale sterilisation using a recognised procedure.
- e. Relying on "exotic" elements like novel chemical substances or hard-to-find excipients is not advised (unless this is a crucial component). Excipients ought to ideally have a history of safe human usage and a drug master file.
- f. Be suitable with packaging or an effective antibacterial preservative.
- g. Be kept ideally without any special requirements.

Table: Different drug absorption and elimination routes in the human eye.^[1]

Absorption area	Drug
Cornea	Lipophilic drug
Conjunctiva, sclera	Lipophilic and hydrophilic drug
From the blood via the blood–ocular barrier	Lipophilic drugs
From the blood via the blood–retinal barrier	Lipophilic drugs
With lacrimal fluid via the trabecular meshwork and Schlemm's canal	Hydrophilic and lipophilic drugs
With lacrimal fluid via venous blood flow to the front uveal tract	Lipophilic drugs
Out of the vitreous humor via the blood–retinal barrier Eback route)	Lipophilic drug
Out of the vitreous humor via the anterior chamber of the eye Efront route)	Hydrophilic and lipophilic drugs

Highlights^[9]

- Since all eye drops of human origin (EDHO) are considered medical products of human origin, strong regulations should be in place regarding donor eligibility, the prevention of infectious disease transmission, uniform labelling, and traceability. Currently, there are regional differences in EDHO production, quality indicators, and regulatory control.
- Because allogeneic EDHO is more uniform and standardised than autologous EDHO, it should be investigated as a substitute.
- While reasonable evidence for the effectiveness of autologous EDHO in the treatment of ocular surface illness that is refractory to conventional treatment exists, high-level evidence (randomised clinical trials) for the use of EDHO remains a priority, especially for allogeneic EDHOs.

**Fig. 1: Human eye Anatomical structure.^[3]**

Drug classes^[1]

The following sheds some light on the possible adverse systemic side effects for some drug classes that are frequently prescribed.

Antibiotics

Although bacterial inflammations of the eye are far less prevalent than other types of inflammation, when they do occur, they can lead to more serious conditions. Antibiotics, which might also have systemic side effects, are used to treat many eye bacterial infections. Since some antibiotics have a broad therapeutic range and may be administered systemically in high dosages, they are utilised to treat posterior parts of the eye that are typically challenging to reach. Topical drugs, such as sulfonamide and sulfacetamide, may cause dermatological adverse effects, such as skin irritation, itching, or rashes.

Corticosteroids

Ophthalmic steroids are medically used to treat acute anterior and chronic posterior uveitis, allergic or noninfectious conjunctivitis, inflammation after cataract surgery, and allergic or noninfectious conjunctivitis. Additionally, they are employed in the treatment of acute giant cell arteritis as well as immunosuppression following transplantation. The significance of steroid medication monotherapy in the treatment of bacterial ocular infections is rather restricted.

Sympathomimetics

Symptoms of noninfectious conjunctivitis or allergy symptoms are frequently treated with vasoactive drugs. During ophthalmological investigations, phenylephrine, a selective 1-receptor, and a weak base at physiological pH, is also used to dilate the pupils.

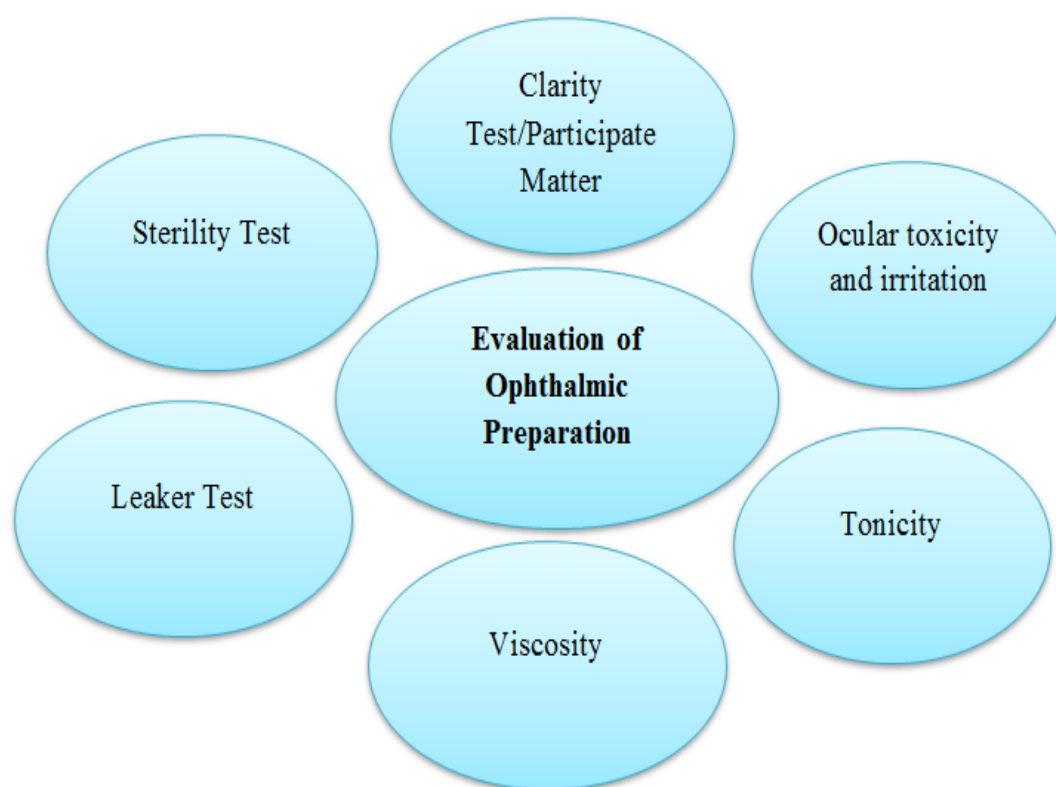
Antisymphotonic agent

The decongestant medication clonidine was the original use for the substance. It was discovered to be efficient at lowering blood pressure during clinical studies. Finally, the pharma manufacturer began marketing it as Catapressan, an antihypertensive medication. Due of its ability to reduce blood pressure when administered intravenously, this medication was frequently utilised in ophthalmology.

Beta-receptor blockers

Glaucoma is still nowadays unfortunately one of the main causes of blindness. The medications most frequently used in the treatment of progressive damage to the optic nerve are beta-blockers. These ophthalmics reduce eye pressure by decreasing the production of intraocular fluid. There are both cardioselective and noncardioselective beta-blockers available on the market. Various dermatological side effects have been reported following topical application of this drug class. Individual patients have reported incidences of urticaria, alopecia, contact dermatitis, or psoriasiform rashes.

Evaluation Test^[10,11,12,3,8]



1. Sterility Test

A sterility test is carried out to detect the presence of a viable form of microorganism in the all-injectable preparation of each lot. Sterility is an absolute requirement of all ophthalmic formulations.

There are two general methods for sterility testing

- 1) Membrane Filtration method
- 2) Direct inoculation method

2. Clarity Test

Ophthalmic solutions must be free from foreign particles, and this is generally done by filtration by membrane filter. The filtration process also helps to achieve clarity of the solution. Particulate Matter: Ophthalmic solutions should be essentially free from particles that can be observed on visual inspection. Ophthalmic preparations that are suspensions, emulsions, or gels are exempt from this test.

3. Tonicity/Iso-tonicity

The term isotonic, meaning equal tone. A solution is said to be isotonic when its effective osmole concentration is the same as that of another solution. In biology, the solutions on either side of a cell membrane are isotonic if the concentration of solutes outside the cell is equal to the concentration of solutes inside the cell. In this case the cell neither swells nor shrinks because there is no concentration gradient to induce the diffusion of large amounts of water across the cell membrane.

4. Viscosity

The most common viscosity desired in an ophthalmic solution is between 25 and 50 cps.

Limitation^[13]

The flow of water in the eye might be different between the Eyes_closed and Eyes_open periods in the imaging protocol. Although one of the five participants had more Eyes_closed periods than Eyes_open periods compared with the other participants, the outflow constant was neither larger nor smaller than the other four, and the effect of having the eyes closed on the flow of water was unclear.

REFERENCE

1. Andre Farkouh, Peter Frigo & Martin Czejka. Systemic side effects of eye drops: a pharmacokinetic perspective. Clinical Ophthalmology, 2022; 2016(10): 2433–2441.
2. Clotilde Jumelle, Shima Gholizadeh, Nasim Annabi, Reza Dana. Advances And Limitations of Drug Delivery Systems Formulated as Eye Drops. Science Direct, 2020; 10(321): 1-22.
3. Chowhan M, Weiner AL. Bhagat H. Encyclopedia of pharmaceutical technology, Drug Delivery. Ophthalmic Route, 3rd ed; USA: Informa Healthcare, 2007; 2: 1220-21.
4. Alejandro Aguilar, Martin Berra, Jorge Trédicce & Alejandro Berra' Efficacy of Polyethylene Glycol–Propylene Glycolbased Lubricant Eye Drops in Reducing

- Squamous Metaplasia in Patients with Dry Eye Disease ' Clinical Ophthalmology, 2022; 2018(12): 1237–1243.
5. Thorsteinn Loftsson, Phatsawee Jansook and Einar Stefansson. Topical Drug Delivery to The Eye: Dorzolamide. Acta Ophthalmol, 2011; 2012(90): 603–608.
 6. Colin P. Churchward, Alia. Al-Kinani, Hamdy Abdelkader, Julian Swinden, Opeoluwa Siwoku, Thinuba Varnakulasingam, Raid G. Alany & Lori A. S. Snyder. Monocaprin Eye Drop Formulation to Combat Antibiotic Resistant Gonococcal Blindness. Scientific Reports, 2020; 10(12010): 1-10.
 7. Gyubin Noh, Taekwang Keum, Jo-Eun Seo, Jaewoong Choi, Bastola Rakesh, Lamichhane Shrawani, Byoungduck Park, Young Wook Choi and Sangkil Lee. Development and Evaluation of a Water Soluble Fluorometholone Eye Drop Formulation Employing Polymeric Micelle. Pharmaceutics, 2018; 10(208): 1-15.
 8. Ar. Satendra Kumar and Dr. Anil Kumar. Formulation, Development and Evaluation of Advance Herbal Ophthalmic Preparation (Eye Drop) Containing Active Constituent from Various Medicinal Plant Source of Different Region of North India. International Journal of Modern Pharmaceutical Research, 2023; 7(5): 191-198.
 9. Christian Gabriel, Denese C. Marks, Reinhard Henschler, Katharina Schallmoser , Thierry Burnouf, Mickey B. C. Koh. Eye Drops of Human Origin—Current Status And Future Needs: Report On The Workshop Organized By The ISBT Working Party For Cellular Therapies. Vox Sanguinis, 2023; 2023(118): 301-309.
 10. Joshi Padamraj Jabki, Khan shahjahan shahdab, Nagre Kaduba Abhishek, Shinde Papi Poonam, Waghulde Vishakha and Nawale Vanashri. Formulation, Development and Evaluation of Herbal Eye Drops Containing Active Ingredients from Multiple Herbs. World Journal of Pharmaceutical Research, 2023; 12(6): 805-820.
 11. Dhoni G. pravin, Dhekale Pallavi, Todkari Rameshwar Reshma, Nibe Nutan, Rai Neeta. 'The Development and Characterization of Eye Drops Containing Acyclovir Microspheres Against Herpes Simplex-Induced Keratitis 'Journal of Pharmaceutics, 2023; 17(1): 71-78.
 12. Kalaria J. Vishwa, S. Saisivam, Anas Alshishani, Jameel S. Aljariri Alhesan, Chakraborty Sumit & Mohamed Rahamathulla. Design And Evaluation of In Situ Gel Eye Drops Containing Nanoparticles of Gemifloxacin Mesylate. Drug Delivery, 2023; 30(1): 1-11.
 13. Moyoko Tomiyasu, Yasuka Sahara, Etsuko Mitsui, Hiroki Tsuchiya, Takamasa Maeda, Nobuhiro Tomoyori, Makoto Kawashima, Toshifumi Nogawa, Riwa Kishimoto, Yuhei Takado, Tatsuya Higashi, Atsushi Mizota, Kohsuke Kudo, Takayuki Obata. Intraocular

Water Movement Visualization Using ^1H -MRI With Eye Drops of O-17-Labeled Saline: First-In-Human Study. *Journal of Magnetic Resonance Imaging* published by Wiley Periodicals LLC, 2022; 57(3): 845-853.