Recent Challenges and Advances in Ophthalmic Drug Delivery System

K. P. Sampath Kumar¹*, Debjit Bhowmik², Shravan Paswan³, Shweta Srivastava⁴

1. Coimbatore medical college, Coimbatore, Tamil Nadu, India
2. Department of pharmaceutical sciences, Karpagam University, Coimbatore, Tamil Nadu, India
3. Advance Institute of Biotech and Paramedical Sciences, Kanpur, Uttar Pradesh, India
4. Hygia Institute of Pharmaceutical Education and Research, Lucknow, Uttar Pradesh, India

Ocular drug delivery is one of the most fascinating and challenging tasks facing the Pharmaceutical researchers. One of the major barriers of ocular medication is to obtain and maintain a therapeutic level at the site of action for prolonged period of time. Ocular drug delivery is hampered by the barriers protecting the eye. The bioavailability of the active drug substance is often the major hurdle to overcome. Conventional ocular dosage form, including eye drops, are no longer sufficient to combat ocular diseases. This article reviews the constraints with conventional ocular therapy, essential factors in ocular pharmacokinetics, and explores various approaches like eye ointments, gel, viscosity enhancers, prodrug, penetration enhancers, microparticles, liposomes, niosomes, ocular inserts, implants, intravitreal injections, nanoparticles, nanosuspension, microemulsion, in situ-forming gel, iontophoresis, and periocular injections to improve the ocular bioavailability of drug and provide continuous and controlled release of the drug to the anterior and posterior chamber of the eye and selected pharmacological future challenges in ophthalmology. In near future, a great deal of attention will be paid to develop noninvasive sustained drug release for both anterior and posterior segment eye disorders. Current momentum in the invention of new drug delivery systems hold a promise toward much improved therapies for the treatment of vision-threatening disorders.

Keyword: Ophthalmic Drug Delivery System

INTRODUCTION: Eye-drops are the conventional dosage forms that account for 90% of currently accessible ophthalmic formulations. Despite the excellent acceptance by patients, one of the major problems encountered is rapid precorneal drug loss. To improve ocular drug bioavailability, there is a significant effort directed towards new drug delivery systems for ophthalmic administration. This chapter will focus on three representative areas of ophthalmic drug delivery systems: polymeric gels, colloidal systems, cyclodextrins and collagen shields. Hydrogels generally offer a moderate improvement of ocular drug bioavailability with the disadvantage of blurring of vision. In situ activated gel-forming systems are preferred as
they can be delivered in drop form with sustained release properties. Colloidal systems including liposomes and nanoparticles have the convenience of a drop, which is able to maintain drug activity at its site of action and is suitable for poorly water-soluble drugs. Among the new therapeutic approaches in ophthalmology, cyclodextrins represent an alternative approach to increase the solubility of the drug in solution and to increase corneal permeability. Finally, collagen shields have been developed as a new continuous-delivery system for drugs that provide high and sustained levels of drugs to the cornea, despite a problem of tolerance. It seems that new tendency of research in ophthalmic drug delivery systems is directed towards a combination of several drug delivery technologies. There is a tendency to develop systems which not only prolong the contact time of the vehicle at the ocular surface, but which at the same time slow down the elimination of the drug. Combination of drug delivery systems could open a new directive for improving results and the therapeutic response of non-efficacious systems. One of the ways to optimize ocular drug delivery is to prolong precorneal drug residence time. This review focusses on recent findings on the formulation effects in ophthalmic drug delivery systems. Some are in common use, some are merely experimental, and others are no longer used. Ocular drug delivery presents unique challenges and opportunities. Eye tissues can be accessed directly with relative ease using topical eye drops. However, the loading and ocular absorption of drugs are limited using traditional solution and suspension formulations, particularly for compounds with low aqueous solubility. For such compounds, delivery to the posterior ocular tissues, including the retina and choroid, can be particularly problematic. The need for formulations that increase the topical ocular absorption of poorly soluble compounds remains largely unmet, precluding the development of otherwise promising medicines for glaucoma, age-related macular degeneration (AMD), diabetic retinopathy, infections, and other eye diseases. Consequently, Bend Research has developed an amorphous nanoparticle platform for topical ocular delivery of low solubility compounds. It enhances the bioavailability of ocular drugs by enabling high drug loadings, increased drug solubility and drug time on the ocular surface, and rapid drug dissolution. These factors produce higher drug concentrations in the primary target tissues—e.g., the irisciliary body (ICB), retina, and choroid—than can be achieved with conventional formulations. In turn, these high concentrations can lead to longer duration of action and decreased dosing frequency. This advance should relax current constraints on new drug discovery for properties such as solubility and lipophilicity and should allow for greater focus on potency and selectivity.
**TYPES:**

1. Aqueous eye drops
2. Oily eye drops
3. Eye ointments
4. Eye lotions
5. Paper strips
6. Ocuserts
7. Hydro gel contact lenses
8. Collagen shields
9. Ophthalmic rods

**ADVANTAGES:**

1. They are easily administered by the nurse
2. They are easily administered by the patient himself.
3. The drug is in a solved state and may be immediately active.
4. They have the quick absorption and effect.

**DISADVANTAGES:**

1. The very short time the solution stays at the eye surface.
2. Its poor bioavailability
3. The instability of the dissolved drug
4. The necessity of using preservatives.

**EYE DROPS**

These are the most common of administering a drug to the eye. All ingredients are completely in solution, uniformity is not a problem

<table>
<thead>
<tr>
<th>TYPES</th>
<th>ADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Solutions</td>
<td>1. Decrease the amount of fluid forming in the eye</td>
</tr>
<tr>
<td>2. Suspensions</td>
<td>2. Increase the ability of the eye to drain fluid</td>
</tr>
<tr>
<td>3. Emulsions</td>
<td>3. Administering medications for the treatment of eye disorders</td>
</tr>
<tr>
<td></td>
<td>4. Preparation for various diagnostic procedures during eye examinations</td>
</tr>
<tr>
<td></td>
<td>5. There is less risk of side effects than with oral medicines</td>
</tr>
<tr>
<td></td>
<td>6. Used during an examination and administered as a local anaesthetic prior to a medical procedure</td>
</tr>
</tbody>
</table>

**EXCIPIENTS USED IN OPHTHALMIC SOLUTIONS**

All raw materials used in the compounding of ophthalmic solutions must be of the highest quality available. Each component must be established and verified for each lot purchased. Excipients used in the product need to be tested for multiple pharmacopoeia specifications to meet global requirement.
When raw materials are rendered sterile before compounding; the reactivity of the raw material with sterilizing medium must be completely evaluated. For raw material components that will not enter as a solution in an appropriate vehicle, particle size must be carefully controlled both before use in the product and finished product specification.

The inactive ingredients in ophthalmic solutions are necessary to perform one or more the following functions

- Adjust concentration and tonicity,
- Buffer and adjust pH,
- Stabilize the active ingredients against decomposition,
- Increase solubility,
- Impart viscosity.

The use of unnecessary ingredients is to be avoided, and the use of ingredients solely to import a color, odour, or flavour is prohibited. The choice of particular inactive ingredients and its concentrations is based not only on physical and chemical compatibility, but also bio compatibility with the sensitive and delicate ocular tissue. The use of inactive ingredients is greatly in ophthalmic products.

**BUFFER SOLUTIONS:**

The pH and buffering of an ophthalmic solution is probably equal importance to proper preservation. The stability of most commonly used ophthalmic solutions is largely controlled by the pH of their environment.

The stability of nearly all products can be enhanced by refrigeration. Except for those few in which a decrease in solubility and precipitation might occur. In addition to stability effect, pH adjustment can influence comfort, safety, and activity of the product. Ideally, would be buffered to a pH of 7.4, considered the normal physiological pH of tear fluid. The pH values of ophthalmic solutions are adjusted within the range to provide an acceptable shelf life. They are buffered adequately to maintain stability within the range for at least 2 years.

A product with a low pH and little buffer capacity that is more comfortable than a similar product with a higher pH and a stronger buffer capacity. The buffer capacity is determined by buffer concentration. If the drug were in acidic moiety, the tears have some buffer capacity of their own, and they can neutralise the pH.

➢ **Selection of phosphate buffers:**

The eye, eyelids and skin surrounding the eye are sensitive to external stimuli; physiological reactions due to deviations outside the near normal values for osmolality or pH are not always seen. However, in a state of ill-health or during regular use of ophthalmic preparations, this situation may be more outspoken.

The active principle in the eye drop can provoke, when not properly dissolved, an irritating or burning sensation leading to lachrymal discharge, occasional haemorrhage or endangering blinking reflexes during surgery.

Lachrymal discharge will cause an unwanted dilution and drainage of medicine. Individual sensitivity may vary and physiological values of tear fluid can fluctuate, which is also dependant on the health condition of the individual eye in general, the nasal corner of the eye being the most sensitive.

Even if the composition of the eye drop approximates the ideal solution, certain (active) principles may cause discomfort to the eye. Non-irritating eye drops should comply with: Sterility, Isotonicity, pH value.

Sterility is of paramount importance when an ophthalmic solution is applied to the injured eye. The character of the active ingredient will to a certain degree determine the above mentioned requirements. The osmotic value of an ophthalmic solution should reflect that of blood, corresponding to a 0.9% sodium chloride solution.
In this respect the physiological term tonicity seems more appropriate than the physicochemical term osmolality. The cornea functioning as selective permeable bio membrane is better accommodating this term.

The osmotic value is commonly expressed in (milli) osmol/liter (osmolarity). This can be transformed to osmolality (mosmol/kg) by dividing by the specific gravity of the solution. Eye irritation must be discerned from an allergy which requires the choice of a different pharmacological agent.

Reasons for buffering an ophthalmic solution:
To prevent unwanted pH changes caused by hydroxyl ion release from the glass in which the solution is stored. In case of a pH-dependent degradation of the active principle, a buffer should be used for stabilization. In case of a pH-dependent solubility, a buffer can be used to dissolve the required amount of drug.

On the other hand there are also limitations to the use of buffers. First of all, the limited buffer capacity of the lachrymal fluid precludes the use of strong buffers outside the pH range of 6.8 - 7.6. In addition, adherence to a pH as close to the physiological pH as possible is important for preventing local precipitations of the drug and minimizing deterioration after administration.

For the formulation of eye drops, phosphate buffer of pH 7.4, used in an eye drop, was chosen as a starting point. The choice for a buffer applied to the ophthalmic solution is determined by the best Compromise of the following issues:

1. It is convenient for patient and surgeon to stay as close as possible to the natural pH of the tear fluid (7.4).
2. The solubility in aqueous solution is problematic at pH values below 7
3. Discomfort for the patient will not be present as long as the pH is between 6.6- 7.8. Tolerability for the cornea is in the pH range of pH 6.6 - 8.5. Changes in permeability will occur outside the pH range of 4 and 10.
4. The permeation of solution increases at lower pH values. On the basis of the above considerations it follows that the optimal pH is between 7.0 - 7.4.

For the present formulation the physiological pH (7.4) was chosen. The often used citrate buffer would have been less favourable, because this buffer composition has hardly any buffering capacity around pH 7.4, in clear contrast to a phosphate buffer.

Interestingly, no difference in pharmacological effect could be demonstrated using ophthalmic solutions in a pH range of 5.0 - 7.5 in preventing disruption of the blood-aqueous barrier. In addition, the use of a phosphate buffer provides stable, single stereoisomer formulations.

Tonicity and Tonicity Adjusting Agents:
It should be adjusting the tonicity of an ophthalmic solution correctly. In compounding an eye solution, it is more important to consider the sterility, stability, and preservative. A range of 0.5% to 2.0% NaCl equivalency does not cause pain and a range of about 0.7%- 1.5% should be acceptable to most persons.

Common tonicity-adjusting ingredients:
1. Sodium chloride
2. Potassium chloride
3. Buffer salts
4. Dextrose
5. Glycerine
6. Propylene glycol
7. Mannitol
PRESERVATIVES USED IN OPHTHALMIC SOLUTIONS

All manufactured ophthalmic solutions be sterile preservatives included as a major component of all multiple-dose eye solutions for the primary purpose of maintaining that sterility in the opened product over its life time of its use. Packaging ophthalmic solutions in the popular plastic eye drop container has reduced, but not completely eliminated, the chances of inadvertent contamination.

There can be a “suck-back” of an unreleased drop when pressure on the bottle is released. If the tip is allowed to touch a non-sterile surface, contamination may be introduced. The plastic eye drop container in order to minimise the hazards of contamination. The cross contamination hazard can be eliminated by the use of packages containing small volumes designed for single application only.

**APPLICATIONS**

Some applications the use of preservatives is not recommended.

- Preservatives should not be used in a corneal storage media.
- Packaging for multidose no preserved preparations
- Drug administered in dry form in offer preserved choice for the formulator

The choice of preservatives is limited only a few chemicals that have been found, to be safe and effective .they are

- Benzalkonium chloride
- Thimerosal
- Methyl and propylparaben
- Phenyl ethanol
- Chlorhexidine
- Polyaminopropyl biguanide

Particularly ophthalmic solutions are preserved with benzalkonium chloride. The limited choice of preservatives agent is further narrowed by the requirement of chemical and physical stability and compatibility with drugs packaging drugs, packaging materials.

To design the formula to fit the requirements of the chosen preservative. The buffer system and excipients can alter preserve action significantly. While it is recognised that excipients themselves may produce toxicity and needs be controlled.

To reduce the largest source of microbial contamination, only sterile purified water should be used in compounding ophthalmic solutions. Pre-packaged sterile water with bacteriostatic agent should not be used.

**GENERAL SAFETY CONSIDERATIONS**

**STERILITY:**

Every ophthalmic product must be manufactured under conditions validated to render it sterile in its final container for the shelf life of the product. Sterility testing conducted on each lot of ophthalmic product by suitable procedures, as set forth in the appropriate pharmacopoeia and each manufacturer’s laboratory. The majority of ophthalmic preparations contain preservatives for multiple-dose use. Sterile preparations in special containers available.

The six methods of achieving sterile products are as follows.

A. Steam sterilization
B. Dry-heat sterilization
C. Gas sterilization
D. Sterilization by ionizing radiation
E. Sterilization by filtration
F. Aseptic processing

For ophthalmic products packaged in plastic containers, typical for ophthalmic products, combinations of two or more of these six methods are used routinely. The aqueous portion of the
composition may be sterilised by filtration. The compounding is completed under aseptic conditions. Sterility may be checked while the finished product is in its bulk form before filling. Sterilization by filtration and aseptic processing has been accepted for preparations that are incompatible with other methods.

**Applications:**

1. They are sterilized by radiation
2. They are non-pyrogenic
3. They are non-toxic
4. Removes the micro-organisms, particles, precipitates and undeserved powders
5. Do not use filters above 45°C
6. Do not use this product if the package is damaged
7. Use laboratory purpose only

1.10.2. STERRILIZATION PROCEDURE:

Those procedures suited best for the extemporaneous preparation of ophthalmic solutions.

**1. Solution in final container**

A. Place the filtered solution in containers that have been washed and rinsed with distilled water.
B. Seal dropper bottles with regular screw caps. The dropper assembly should be stapled in to a paper envelop.
C. Sterilise 20 min at 15 psi (121).
D. Do not assemble until use.

**2. Dropper bottles**

A. Wash container thoroughly and rinse with distilled water.
B. Loosen caps and place bottle in autoclave.
C. Autoclave 15 min at 15 psi (121).
D. Partially cool autoclave.
E. Remove bottles from autoclave and secure caps.
F. Store sterilized bottle in a clean dustproof cabinet.

**3. Glassware and equipment**

A. Wrap adapters (containing filters), syringes, glasswares, spatulas, etc, in autoclave paper secure with masking tape.
B. Place article in autoclave and sterilise.
C. Store in separate cabin until ready to use.

**4. Microbiological filtration**

A. All equipment and glassware as well as stock solutions should be sterile.
B. Unwrap sterile syringe and draw prepared solution in to syringe.
C. Unwrap sterile adapter containing bacterial filter and attach to syringe.
D. These are available as single-filtration, pre-sterilized, disposable units and should be used whenever possible.
E. Force solution filter directly in to sterile container.
F. By employing automatic filling outfit, more than one container of the same prescription can be prepared.
G. Cap container immediately.

The procedure outlined above should be carried out in a clean area equipped with ultraviolet lighting and preferably in a laminar-flow hood.

**Laminar-Flow principle:**

A Laminar-Flow work area is a particularly convenient means of preparing sterile, particulate free solutions. Laminar-flow is defined as air floe in which the total body of air moves with uniform velocity along parallel lines with a minimum of eddies. Luminaries minimizes the possibility of airborne microbial contamination by providing air free of viable particles and free of practically all inert particulate. Laminar-flow units are available in a variety of shapes and sizes and in two broad categories, horizontal and vertical laminar flow.
MANUFACTURING ENVIRONMENT

Aside from drug safety, stability, efficacy and shelf-life consideration associated with tonicity, pH, and buffer capacity. The major design criteria of an ophthalmic solution are the additional safety criteria of sterility, preservation efficacy, and free from extraneous foreign particulate matter. These environmentally controlled must meet the requirement of class 100,000 space in all areas where open contain and closures are not exposed, or where product filling and capping operations are not taking place. Often there design criteria are coupled with laminar air flow concepts.

MANUFACTURING TECHNIQUES

Aqueous ophthalmic solutions are manufactured by methods that call for the dissolution of the active ingredient and all or portion of the excipients in to all or a portion of the water and sterilization of this solution by heat or by sterilizing filtration through sterile depth or membrane and filter receptacle.

If complete at this point, such as previously sterilized solutions of viscosity-imparting agents, preservatives, and so on, and the batch is brought to final volume with additional sterile water.

PACKING MATERIALS

Eye drops have been packaged almost entirely in a plastic dropper bottle. The designed plastic dropper bottle is convenience of use by the patient, decreased contamination potential, lower weight, and lower cost.

The plastic bottle has the dispensing tip as an integral part of the package. The plastic bottle and dispensing tip is made of low density polyethylene (LDPE) resin. The LDPE resins used are compatible with a very wide range of drugs and formulation components. The plastic dropper bottles are also permeable to water.

The disadvantage is their sorption, leaching and permeability characteristics. This can be achieved by using a resign containing an opacifying agent such as titanium dioxide, by placing an opaque sleeve over the containers.

If the drug is light sensitive, additional package protection may be required. Use of an ETO (ethylene oxide) sterilized PE, PP and/or PET container to improve the stability of an aqueous pharmaceutical composition, in particular to improve the stability of a composition being susceptible to oxidative degradation.

OPHTHALMIC DRUG DELIVERY SYSTEM

Eye is the most easily accessible site for topical administration of a medication. Drugs are commonly applied to the eye for a localized action on the surface or in the interior of the eye.

Eye is most interesting organ due to its drug disposition characteristics. For ailments of the eye, topical administration is usually preferred.
over systemic administration, before reaching the anatomical barrier of the cornea, any drug molecule administered by the ocular route has to cross the precorneal barriers.

These are the first barriers that slow the penetration of an active ingredient into the eye and consist of the tear film and the conjunctiva. The medication, upon instillation, stimulates the protective physiological mechanisms, i.e., tear production, which exert a formidable defence against ophthalmic drug delivery.

Another serious concomitant of the elimination of topically applied drugs from the precorneal area is the nasal cavity, with its greater surface area and higher permeability of the nasal mucosal membrane compared to that of the cornea.

Normal dropper used with conventional ophthalmic solution delivers about 50-75µl per drop and portion of these drops quickly drain until the eye is back to normal resident volume of 7µl. Because of this drug loss in front of the eye, very little drug is available to enter the cornea and inner tissue of the eye.

Actual corneal permeability of the drug is quite low and very small corneal contact time of the about 1-2 min in humans for instilled solution commonly lens than 10%. Consequently only small amount actually penetrates the cornea and reaches intraocular tissue.

Ideal ophthalmic drug delivery must be able to sustain the drug release and to remain in the vicinity of front of the eye for prolong period of time. Consequently it is imperative to optimize ophthalmic drug delivery.

**Characteristics are required to optimize ophthalmic drug delivery system:**

- Good corneal penetration.
- Prolong contact time with corneal tissue.
- Simplicity of instillation for the patient.
- Non irritative and comfortable form.

**Figure No. 1. Ocular drug delivery system.**

**Modes of Transport**

Passive transport or simple of diffusion of molecules is a transport process dependent on water and lipid solubility, size of the molecules, and concentration gradient across the cellular membrane. No energy is expended in the process, and transport will cease when the concentration of the molecule on both side of the membrane are equal.

Passive transport is not inhibited by metabolic inhibitors (inhibiting ATP production or utilisation) or by competitive substrates. Hydrophilic molecules pass through pertinacious pores in the cellular membrane and lipophilic molecules diffuse through the lipid portion of the membrane. Transport through the pores is limited by the pores size i.e. specific to each tissue. The low lipid solubility of ionised molecules may be increased by altering the degree of ionisation is changes in the solution pH. Passive transport is an energy-dependent process requiring ATP, is carrier-mediated, and is capable of transporting substrates against a concentration gradient.

Macromolecular carriers are membrane-bound and have varying degrees of substrate specificity. The carrier reversibly binds to substrate; transport
releases the molecule on the other site of the membrane, and returns to the original state. These characteristics also make active transport subject to metabolic inhibitors, competitive inhibition from other similar substrates, and saturation at high substrate concentrations.

Active transport in the corneal endothelium is essential to maintainance of proper stromal hydration. Facilitated transport combined some properties of both mechanisms discussed above. This type of transport is carrier mediated so that there is substrate specificity, a transport maximum, and competitive inhibition.

However, facilitated transport is not energy-dependent unable to transport substrate against a concentration gradient.

**Physiological barriers:**

The structure of the outside of the eye and cross section of the anterior segment of the eye. The front part of the globe of the eye is clear and colourless and is called the cornea. It contains no blood vessels, but is rich in nerve endings. The cornea consists of three major layers:

- The Outer epithelium
- Middle stroma
- Inner endothelium.

When topically applied solutions are administered to the eye, they first encounter of the cornea and conjunctiva, representing the primary barriers to drug penetration. Making them barriers to the permeation of polar, water-soluble compounds. The stroma, on the other hand, is a hydrophilic layer containing 70 to 80% water, presenting barrier to the permeation of non-polar, lipid soluble compounds. The other parts of the boundary layer to the front of the eye are the sclera. This is white in colour and opaque, and contains most of the blood vessels supplying the anterior tissue of the eye. The outer surface of the sclera is loosely covered by the conjunctiva membrane, which is continuous with the inner surface of the eyelids, and also presents a significant permeability barrier to most drugs. For drugs that permeate the vascular system of the sclera and conjunctiva, transport tends to be away from the eye into the general circulation.

Other major physiological barrier mechanisms are due to tear production and the blink reflex. The conjunctiva and the corneal surface of the eye are continuously lubricated by a film of fluid secreted by the conjunctiva and lachrymal glands. The lachrymal secrete a watery fluid called tear, and the sebaceous glands on the margin of the eye lids secrete an oily fluid which spreads over the tear film. The later reduces the rate of evaporation of the tear film from the exposed surface of the eyes.

Upon administration of topically applied eye-drops, removal from the eye is rapid due to tear production and the blinking process occurring simultaneously. The precorneal volume is about 7µl, but the volume up to 20 to 30 µl can be held in this area before spillage occurs. Installation of volumes greater than will simply spill out on to the cheek or will be rapidly lost with the tears through drainage in to the nasal-lachrymal duct.

The introduction of any eye-drop product, but particularly products causing irritation, is likely to stimulate the tear production rate and increase the rate of drug removal from the eye. The removal of material by dilution is also aided by the blink reflex where each blink pumps approximately 2 µl.
VARIOUS TYPES OF DRUGS USED FOR OPHTHALMIC DISEASES

Table No. 1. Drugs for ophthalmic diseases

<table>
<thead>
<tr>
<th>S. NO</th>
<th>DISEASE</th>
<th>PRODUCT</th>
<th>BRAND NAME</th>
<th>MFG BY</th>
<th>DOSAGE FORM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammation</td>
<td>Ketorolac</td>
<td>ACUVAIL</td>
<td>Allergan</td>
<td>Eye-drops</td>
</tr>
<tr>
<td>2</td>
<td>Inflammation</td>
<td>Diclofenac</td>
<td>VOLTARIN</td>
<td>Novartis</td>
<td>Eye-drops</td>
</tr>
<tr>
<td>3</td>
<td>Infection</td>
<td>Chloramphenicol</td>
<td>CHLOPTIC</td>
<td>Allergan</td>
<td>Eye-drops</td>
</tr>
<tr>
<td>4</td>
<td>Miotics</td>
<td>Pilocorpin Hcl</td>
<td>PILOPINI</td>
<td>Alcon</td>
<td>Gel</td>
</tr>
<tr>
<td>5</td>
<td>Viral</td>
<td>Ganciclovi</td>
<td>ZIRGAN</td>
<td>Alliance</td>
<td>Gel</td>
</tr>
<tr>
<td>6</td>
<td>Infection</td>
<td>Gatifloxacin</td>
<td>ZYMAR</td>
<td>Allergan</td>
<td>Eye-drops</td>
</tr>
<tr>
<td>7</td>
<td>Inflammation</td>
<td>Dexamethasone</td>
<td>TOBRADEX</td>
<td>Alcon</td>
<td>Eye Ointment</td>
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<tr>
<td>8</td>
<td>Glaucoma</td>
<td>Laxobetolol Hcl</td>
<td>BETAXON</td>
<td>Alcon</td>
<td>Eye-drops</td>
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<tr>
<td>9</td>
<td>Inflammation</td>
<td>Flurometholone</td>
<td>BETAXON</td>
<td>Alcon</td>
<td>Eye-drops</td>
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<td>10</td>
<td>Conjunctivitis</td>
<td>Ciprofloxacin</td>
<td>FML</td>
<td>Allergan</td>
<td>Suspension</td>
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<tr>
<td>11</td>
<td>Conjunctivitis</td>
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CONCLUSION

Ocular drug delivery has been a major challenge for scientists due to its unique anatomy and physiology which contains various types of barriers such as different layers of cornea, sclera and retina including blood aqueous and blood–retinal barriers, choroidal and conjunctival blood flow etc. These barriers cause a significant challenge for delivery of a drug alone or in a dosage form, especially to the posterior segment of the eye. To overcome these problems various types of dosage forms such as nanoparticles, nanomicelles, liposomes and microemulsions have been developed. Novel drug delivery strategies such as in situ gels were developed to sustain drug levels at the target site for a sufficient time. Drug delivery via ophthalmic route has proved significant advancement for future perspectives.

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