RESEARCH ARTICLE ON FORMULATION AND ASSESSMENT OF LEVOFLOXACIN OPTHALMIC EMULGEL

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ABSTRACT:

This review paper provides an overview of the formulation and assessment of levofloxacin ophthalmic Emulgel to extend resident duration in ocular tissues, decrease instillation time, and improve patient compliance and thereby reducing bacterial infection. Emulgel feature a double release system, i.e., gel and emulsion, making them accessible delivery systems. A synthetic, broad-spectrum antibacterial drug called levofloxacin is used to treat a number of bacterial illnesses, including bacterial conjunctivitis and otitis media. Quinolone antibiotics like levofloxacin are classified as class-I biopharmaceuticals. Different polymers, including xanthan gum, sodium alginate, and methyl cellulose, can be combined with gel to create levofloxacin ocular Emulgel. Evaluations of the created ocular Emulgel pH, spread abilityS, swelling index, viscosity, and medication content are possible. An evaluation of the generated ocular emulgel's pH, spreadability, swelling index, viscosity, drug content, centrifugation, antibacterial activity, and in-vitro drug release and stability study is possible. FT-IR and DSC tests can be used to determine whether a drug is compatible with its excipients.

Conclusion: Levofloxacin ocular emulgel may be a superior method of formulation for antibacterial activity.

The end of this review composition is to investigate optical emulgel, a nobel prize-winning methodof delivering levofloxacin for the treatment of bacterial infections of the eye.

KEYWORDS: Conflation, Double release system, levofloxacin, Ocular emulgel.

INTRODUCTION

Emulgel being a new technologies in nobel DDS used locally having characteristics of double control release i.e. emulsion as well as a gel. Emulgels incorporates a double release system i.e. gel and conflation thus are accessible delivery systems. Once gel and conflation are employed ina combined type, it's stated as emulgel. Emulgel is employed to treat pangs and pains caused bycold, headaches, muscle pangs, backaches, arthritis, and different conditions and injuries.[1] The

patient's adherence to topical phrasings is critical concerning habitual skin conditions, like acne, skin infections, and psoriasis. Topical medicine administration could be a localized medicine delivery system anyplace within the body through ophthalmic, rectal, vaginal, and skin as topicalroutes. They are using a wide range of treatments for their skin, both healthy and pathogenic, for cosmetic and dermatological purposes. These formulations place chemistry nature from solid through circumfluous to liquid. Medicine substances are hardly administered alone, still kindly asa part of a formulation, together with one or a lot of non-medicated agents that serve a varied andspecific pharmaceutical operation. Medicine is administered local action at the situation of application or general effects. If the drug substance is in solution or have a good O/W partition coefficient and if it's a nonelectrolyte , it results to enhanced drug absorption through the skin. Pharmaceutical preparations that are applied to the skin are primarily intended to have a local effect and are designed to offer extended local contact with limited systemic drug absorption. Drugs applied to the skin for local action include antifungal agents, antiseptics, protectants, and skin emollients. Bypassing first-pass metabolism is the major advantage of a topical delivery system. Avoidance of the risks and inconveniences of therapy and the multitudinous conditions of absorption like pH changes, presence of enzymes, and gastric emptying time are different benefits of topical preparations.[1,4]

Rationale of emulgels as a new formulation:

Topical treatments like cream and ointment have a number of drawbacks, including less spreading constant, poorer stratum corneum penetration, slower penetration, less patient compliance due to viscosity, and the need for vigorous application. Gels also have the drawback of transporting drugsthat are hydrophobic. Here, emulgel is chosen based on the solubility research of the antimicrobialagent in them and the emulsifier; as a result, the drug's solubility may be solubilized in emulgel, which may penetrate through the stratum corneum to act on the skin's live soft tissue. Less dosageof the medicine may have significant pharmacologic activity because drug globules may permeatethe stratum corneum to an extent that is more accessible for drug action.[2]

Additionally, selecting different excipients might help pharmacologic action in one or both of ourways. Edges of both an emulsion and a gel may be offered by emulgel. Emulgel will boost the amount of medication that is deposited on the skin. The emulsion has a higher bioavailability thanemulgel, but stability is an issue, and patient compliance is also lower. Emulgel thus has many advantages over ointments and gels.[2,4]

Need for study:

The goal of the project is to create a levofloxacin ocular emulgel using sodium alginate, Xanthan gum, and methyl cellulose as the gelling agent for ocular delivery. This will shorten the time needed for instillation, prolong the drug's residence in the eye, and improve patient compliance while also lowering the risk of bacterial infection. Several bacterial infections are treated with levofloxacin. Levofloxacin is categorized as a class-I biopharmaceutical substance. This medicine is a member of the quinolone antibiotics drug class. It stops bacteria from growing. Only bacterialillnesses are treated by these antibiotics. Due to their homogeneous behavior and jelly-like consistency, pharmaceutical semisolid dosage forms, particularly

emulgels, have attracted the attention of scientists and industry researchers over the past ten years.

Emulgels are colloidal systems blended with oil-in-water solutions as an inner phase. They are often referred to as o/w emulsion gels or cream gels. Emulgels have been extensively studied as apromising drug delivery system for the administration of lipophilic medicines. The goal of this research was to create a Levofloxacin emulgel formulation using Carbopol 934, Xanthan gum, andHPMC K100 as the gelling agent for ocular delivery. The ideal option for topical treatment of ocular illnesses is an eye drop solution, particularly in some circumstances where a localized pharmacological action (for example, on the cornea and/or anterior chamber) is required. Drug retention period is so short due to self-protective mechanisms such lacrimal secretion, the blink reflex, and corneal impermeability that repeated injection is required for very effective therapy.

Formulations with a higher viscosity have been researched in order to prevent the quick dilution. The therapeutic efficacy of a medicine may be improved by lengthening both its absorption and residence time in the precorneal region. Hence, it is envisioned to prepare Levofloxacin ocular emulgel and evaluate the in-vitro studies.[4,5]

Types of emulgels:

- **Macroemulsions gel:** These are the most prevalent kinds of emulgels, and they have emulsion droplet sizes larger than 400 nm. Although they are seemingly opaque, amicroscope makes the individual droplets plainly visible.
- **Microemulsion:** Since the droplet size of micro-emulsions ranges from 100 to 400 nm andthey do not coalesce, they are transparent and thermodynamically stable. In certainproportions, water, oil, surfactant, and cosurfactant make up micro-emulsions.
- **Nanoemulgel :** Nano-emulgel is the term used when nano-emulsions are combined with gel. An interfacial coating of surfactant and co-surfactant molecules with a globule size ofless than 100 nm stabilizes transparent thermodynamically stable nano-emulsions of oil and water. In vitro and in vivo, nanoemulsion formulations have established transdermal and dermal delivery qualities. In comparison to more traditional topical formulations like emulsions and gels, nano-emulsions have increased the transdermal penetration of numerous medications.

Advantages of Emulgels

- Using an o/w emulsion, hydrophobic drugs can be easily integrated into the gel.
- Better loading capacity.
- Economical.
- Controlled ejection.
- Boost the formulation's stability.
- Extend the drug's mean residence time and duration of contact.
- Dual drug release from gel and emulsion.
- Emulgels are employed in cosmetic applications as well.

Disadvantages of Emulgel

- While making the emulgel, bubbles formed.
- The potential for allergic responses.

- Drugs with large particle sizes (>400 Daltons) do not easily penetrate the skin barrier or be absorbed.

Formulation approaches of ocular emulgel .

I. ***Aqueous material :***This forms the aqueous phase of the emulsion. Alcohol and water are frequently employed as agents..

II. ***Oils:*** These substances shape the emulsion's oily component. Because they operate as the drug's delivery system and have occlusive and sensory properties, mineral oils— either alone or in combination with soft or laborious paraffin—are frequently employedin emulsions for external application. Widely utilized oils in oral preparations include fish liver oils, non-biodegradable mineral and castor oils, which have local laxative effects, and numerous fastened oils of vegetable origin (such as Arachis, cottonseed, and maize oils), which are employed as nutritional supplements.

III. ***Emulsifiers:*** Emulsifying agents are used to promote emulsification during productionand to control stability over a period that can range from days for emulsions that are ready on-the-spot to months or years for industrial preparations. For instance, sorbitanmonooleate (span 80), polyoxymethylene sorbitan monooleate (tween 80), octadecanoic acid, and atomic number 11 stearate and synthetic resin glycol forty stearate are the examples.

IV. ***Gelling agent:*** These substances can be employed as thickening agents as well as to raise the consistency of any dosage form.

V. ***Permeation enhancers:*** These substances enter the skin and interact with its components to cause a temporary and reversible increase in skin porosity.

Properties of penetration enhancers

1. They must be non-allergenic, non-toxic, and non-irritating.
2. They should preferably operate quickly, thus the action and duration of the effect should bothbe certain and repeatable.
3. They must not bind to receptor sites or have any medicinal function within the body.
4. In order to allow therapeutic medicines to enter the body while avoiding the loss of endogenousmaterial from the body, the penetration enhancers must function unifacially.
5. The penetration enhancers should be able to be formulated into different topical treatments andshould work well with both excipients and medications.
6. They must have a suitable skin "feel" and appropriate cosmetics.

Mechanism of penetration enhancers

There are three major ways penetration enhancers can work:

1. Diruption of the highly organised structure of stratum corneum lipid.
2. Interaction with intercellular protein.
3. Improved partition of the drug, co-enhancer, or solvent into the stratum corneum.

Alteration in one of three pathways is how the enhancers work. The modification of the polar route requires a solvent-induced protein conformational change. The fluidity of the lipid-protein component of the stratum corneum was increased by the fatty acid enhancers. Some enhancers

modify the multi-laminate pathway for penetration, affecting both polar and non-polar pathways.Enhancers can increase diffusivity of drug through skin proteins. The design and development of the product are significantly impacted by the sort of enhancer used.(2)

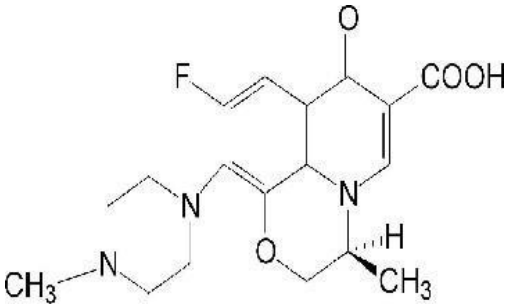
MATERIALS AND METHODS:

- **Drug:** Levofloxacin
- **Gelling agents:** Sodium alginate, Xanthan gum, Methyl cellulose
- **Excipients:** Oil Phase : Caster oil
  Viscosity enhancers,
  Emulsifying agents: Poloxamer 188 Preservatives : Benzalkonium ChlorideIso osmotic 3% glycerin

DRUG PROFILE :

(a) Levofloxacin: Levofloxacin, is a synthetic broad-spectrum antibacterial agent and a chiral fluorinated carboxyquinolone, is the pure (-)-(S)-enantiomer of the racemic drug substance ofloxacin. The chemical name is (-) -(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4- methyl-1-piperazinyl)-7-oxo7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemi hydrate.

Structural form:



Description: Levofloxacin is a light yellowish-white to yellow-white crystal or crystalline powder.

Empirical formula: C18H20FN3O4 • ½ H2O

Systematic IUPAC Name: 9-fluoro-2,3-dihydro-3-methyl-10-(4-methylpiperazine-1-yl)-7-oxo-7H-pyridol[1,2,3-del]-1,4-benzoxazine-6-carboxylic acid

Molecular formula: C18H2OFN3O4

Molecular Weight: 370.38

Chemical Properties:

Solubility: The information shows that levofloxacin's solubility (about 100 mg/mL) is practicallyconstant between pH values of 0.6 and 5.8. In this pH range, levofloxacin is thought to be solubleto readily soluble. Above pH 5.8, solubility rises quickly until it reaches a maximum at pH 6.7 (272 mg/mL), and this range is thought to be easily soluble. The solubility falls above pH 6.7 andreaches its lowest point (about 50 mg/mL) at about pH 6.9.

Melting point: 226ºC

Clinical Pharmacology

Mechanism of action: Levofloxacin is the L-isomer of the quinolone antibacterial racemate ofloxacin. The L isomer of ofloxacin is where most of its antibacterial action is found. Levofloxacin and other fluoroquinolone antimicrobials work by inhibiting the enzymes needed for DNA replication, transcription, repair, and recombination—bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases). Anti-bacterial spectrum the materials have broad spectrum antibacterial and antifungal powerful features, the majority of Enterobacteriaceae bacteria such Klebsiella pneumoniae, Proteus is, typhoid Salmonella spp, Shigella species, some E. coli, and has strong antibacterial activity, part of staphylococcus, streptococcus pneumonia, influenza bacillus, Pseudomonas aeruginosa, gonorrhea, and chlamydiahave good antibacterial effect.

Dosage and Administration:

As an ophthalmic solution, levofloxacin is given topically to the eye. Levofloxacin should be used orally every two hours up to eight times for the first two days to treat bacterial conjunctivitis, followed by every four hours up to four times for the following five days.

Common adverse effects:

Transient decrease in vision, transient ocular blurring, ocular pain or discomfort, foreign body sensation, headache, fever, pharyngitis, and photophobia occur in 1-3 % of patients.Allergic reactions, lid edema, ocular dryness, and ocular itching occur in less than 1% of patients.

Contraindications: Known hypersensitivity to levofloxacin, other quinolones, or any ingredientsin the formulation.

Drug Interactions: The systemic absorption may occur following topical application of levofloxacin to the eye. The reported interactions with theophylline, caffeine, anti coagulants andcyclosporine.

Indication: Conjunctivitis & otitis media.

Storage : Levofloxacin should be stored between 15-30º C (59-86 F).

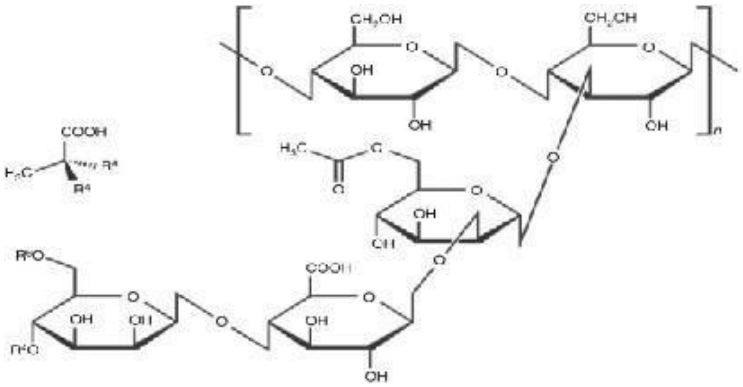
Polymer Profile

(b) Xanthan gum

Synonyms: Cornsugargum; E415; Grindsted; Keldent; Keltrol; Rhodicare S; Rhodigel; polysaccharide B-1459; Vanzan NF; xanthan gummi; Xantural

Description : It is derived from Xanthomonas campestris. It appears as a thin, odorless

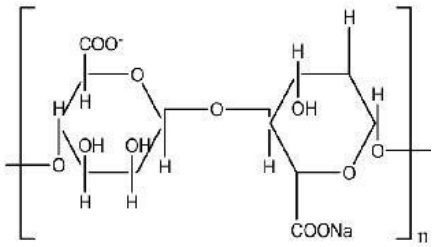
powderthat is either white or cream in color and free to flow..
Empirical Formula: C35H49O29
Structural form:



Solubility: In ethanol and ether, it basically is insoluble; in cold or warm water, it is soluble.
Functional categories: Gelling agent; stabilizing agent; suspending agent; sustained-releaseagent; viscosity-increasing agent.
Melting point: 270ºC
Storage conditions : It needs to be kept in a tightly closed container in a cold, dry location.
Incompatibilities: Incompatible with oxidizing agents, some active substances such amitriptyline, tamoxifen, and verapamil as well as some tablet film coatings, carboxymethylcellulose sodium, and dried aluminum hydroxide gel.
Safety: It is non-toxic and non-irritant. Acceptable dose by WHO is 10mg/kg body weight.
Applications: It is widely employed as a suspending and stabilizing agent, as well as a thickeningand emulsifying agent, in oral and topical medicinal formulations, cosmetics, and foods.

(c) Sodium alginate

Synonyms: Algi, alginic acid, sodium salt
Chemical name: Sodium alginate, Alginic acid monosodium salt
Empirical formula: C_6 H_9Na O_7
Structural form:



Molecular weight: 216.12g/mol
Description: Sodium alginate is a chelating agent made from the sodium form of alginic acid andgum derived primarily from the cell walls of brown algae. Sodium alginate binds to and inhibits the intestinal absorption of various radioactive isotopes, including radium Ra 226 and

strontium Sr 90, when taken orally. Sodium alginate occurs a white to yellowish white powder and is almostodorless. Sodium alginate is a slowly soluble in cold water, insoluble in alcohol and other organicsolvents viz. chloroform and ether.

Uses: As an auxiliary fining agent and foam stabilizer in the brewing industry. Calcium sodium alginate-based antiperspirant. Used in industry and medicine (textiles, food additives, cosmetics, pharmaceuticals and other emulsifiers and so on) A solid medium that is used to grow bacteria and other micro- organisms. Agent in silver recovery from waste photographic solution; pharmaceutical tablet binding agent; protective colloid in boiler feed water compounds; thickener for dye solution in the textile industry; base for dental impression material; agent in silver recoveryfrom waste photographic solution; bodying agent for bakery products.

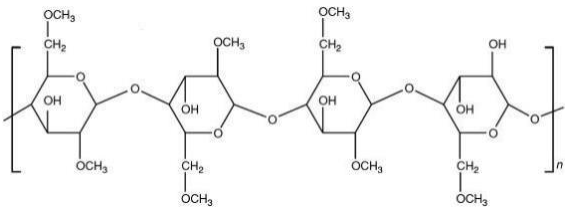
(d) Methyl Cellulose

Synonyms : Cellulose methyl ether, methyl cellulose

Description: Chemically, cellulose is the source of methyl cellulose It is sold under a number oftrade names and is used as a laxative that forms a bulk as well as to thicken and emulsify a numberof food and beauty products. Similar to cellulose, it cannot be digested and is neither toxic nor allergic.

Empirical Formula : C6H7O2(OH)x(OCH3)

Structure



Molecular Weight 454.5

Solubility : 5 to 10 mg/mL at 63° F

Uses: This medication is used to treat constipation It gives your feces more weight, which promotes bowel movement. Additionally, it works by adding more water to the stool, which makes it softer and simpler to pass.

PREFORMULATION STUDIES:

Preformulation study is the first step in the development of dosage form of drug substance it is defined as a phase of research and development where the biopharmaceutical principles are appliedto determine the physiochemical parameters of a new drug substance.

Objective of Pre-formulation studies

- To generate useful information about the drug to the formulator to design an optimum drug delivery system.
- To establish a new medicinal substance's essential physicochemical characteristics.
- To establish physical characteristics of the drug
- To find out solubility and melting point of pure drug(Levofloxacin).

- To find out the drug compatibility with commonly used excipient by FTIR and DSC method.

PREPARATION AND CHARACTERISATION OF LEVOFLOXACIN OCULAR EMULGEL.

Typically, ocular emulgel is created in three phases, which are as follows:

- **Step-1:** Preparation of emulsion phase: -
  Levofloxacin is dissolved in castor oil to create the oil phase, which is then used tocreate the O/W emulsion phase. Levofloxacin 500 mg is dissolved in 3 gm of castor oil. Thenafter, Poloxamer 188(an emulsifying agent) and benzalkonium chloride(a preservative) are then dissolved in distilled water to create the aqueous phase. Using a hot plate magnetic stirrer, the oil and aqueous phases are both heated to 70°C. After heating, the oil phase is dispersed in the aqueous phase with constant stirring at 1500 rpm until a homogenous emulsion is created.
- **Step-2:** Preparation of gel phase: -
  The gel phase is prepared by dissolving the gelling agent in iso-osmotic containing3% glycerin solution. Different gelling agents will be used at different concentrations for the preparation of gel phase.
- **Step-3:** Formation of emulgel:-
  The final emulgel is created by mixing the emulsion and gel phase at a weight ratioof 1:1 for 15 minutes at a speed of 1500 rpm. This produced a smooth, homogenousemulgel.

Table 01: Formulation of Levofloxacin Ocular Emulgel

Sl.no.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
01.	Levofloxacin (mg)	500	500	500	500	500	500	500	500	500
02.	Sodium alginate (mg)	500	-------	-------	750	-------	-------	1000	-------	-------
03.	Methyl cellulose (mg)	-------	500	-------	-------	750	-------	-------	1000	-------
04.	Xanthan gum (mg)	-------	-------	500	-------	-------	750	-------	-------	1000
05.	Castor oil (gm)	3	3	3	3	3	3	3	3	3
06.	Poloxamer (mg)	660	660	660	660	660	660	660	660	660
07.	Benzalkonium chloride(ml)	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
08.	Iso osmotic 3% glycerin (ml)	49	49	49	49	49	49	49	49	49
09.	D.Water(ml)	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml	Up to 100ml

EVALUATION OF LEVOFLOXACIN OCULAR EMULGEL .

Physical properties:

The prepared emulgel formulation's physical characteristics need to investigated. We look at phaseseparation, color, homogeneity and consistency.

pH determination :

A pH meter is used to measure the pH of the emulgel. it can be done by inserting the electrode tip into the emulgel and the result was recorded two minutes later.

Rheological study:

Using a Brookfield viscometer (Brookfield LV, spindle no. 64), the viscosity of the prepared emulgels is assessed. The emulgel sample was placed in a glass container, and the viscometer's spindle is allowed to rotate at pre-set speeds (5, 10, 20, 30, 50, 60, and 100rpm). After 30 seconds, the viscosity for each speed is noted.

Drug content determination:

One gram of emulgel sample was dispersed in 100 ml phosphate saline buffer pH 7.4 and sonicated for 2 h. The sonicated mixture was filtered via a 0.45 m Millipore filter before being subjected to UV analysis.

Swelling Index:

To determine the emulgel's swelling index, 1 gram of the gel is placed on a piece of porous aluminum foil and then placed separately in a 50 ml beaker with 10 ml of 0.1 N NaOH. Following that, samples were retrieved from beakers at various intervals and placed on a dry surface for a while before being reweighed. Swelling index is calculated as follows:

Swelling Index (SW) % = [(Wt. – Wo) / Wo] × 100.

Where, (SW) % = Equilibrium percentage swelling,Wt. = Weight of swelled emulgel after time t.

Wo = Initial weight of emulgel at zero time

Spreadability:

The apparatus suggested by Multimer et al (1956) that is suitably modified in the lab andused for the study is used to measure spreadability. It is made up of a wooden block that has a pulley at one end. This method is based on the 'Slip' and 'Drag' properties of emulgelsand used to measure spreadability. A ground glass slide is fixed on this block. An excess of emulgel (about 2 gm) under study is placed on this ground slide.The emulgel is then placed in a sandwich between this glass slide and another glass slide with a hook and a fixed ground slide dimension. For five minutes, a 1 kg weight is placed on top of each slideto release air and to provide a uniform film of the emulgel between the slides. The edges are scrapped to clean the extra emulgel. A pull of 80 grams is then applied to the top plate.With the aid of the string that is bound to the hook, the time (in seconds) it takes the top slide to travel 7.5 cm is recorded. A shorter interval indicates better spreadability.

Spreadability (S) = M.L/T

Where, M = Weight added to upper slide, L = Length of glass slides T = Time taken to totally separate the slides from one another.

Centrifugation study:

This study was carried out using a minicentrifuge running for 30 minutes at 3000 rpm. This methodis used to determine the stability of emulgel and is done only after one week of formulation.

Antibacterial activity :

Muller Hinton agar plate can be used to study invitro antibacterial activity of the formulation. To prepare Muller Hington agar plate, 28 g of powder is dispersed in 1 l of deionized water, mixing it thoroughly and sterilizing it in an autoclave at 15 lbs. pressure (121°C) for 15 minutes. After cooling it to 47°C, the medium is then poured into sterile plates in a septic environment and allowed to solidify at room temperature. Two different types of bacteria(Escherichia coli and Staphylococcus aureus) are tested. Over the surface of the medium, precisely 0.1 mL bacterial suspension having a uniform turbidity (106 CFU/mL) is distributed gently with a sterile glass spreader. The cork borer used to create

the wells had a 6 mm diameter. Levofloxacin ocular emulgel and an adequate amount of the ideal formula were injected into the pore of each of these plates using a syringe, and the plates were then incubated at 37°C for 24 hours. The inhibitory zones' diameter were measured in millimeters.

***In Vitro Release* Study:**

Franz diffusion cell (with effective diffusion area 3.14 cm^2 and 15.5 ml cell volume) is used for the drug release studies. Emulgel of 200 mg is equally placed to the eggmembrane's surface. The egg membrane is clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber is filled with freshly prepared PBS (pH 5.5) solution to solubilize the drug. Magnetic stirrer is used to stir the receptor chamber. Atappropriate intervals, the samples (1.0 ml aliquots) are collected. Samples are analysed for drug content by UV visible Spectrophotometer after appropriate dilutions. To determine the overall amount of drug release at each time period, cumulative adjustments are done. As a function of time, the total amount of medication released across the egg membrane isthen calculated.

Stability Studies:

Stability study is performed to check any considerable changes that may occur in formulation during its storage. All the formulation are kept for 3 months at room temperature. Stability of the formulation is evaluated by determining their pH, Spreadability, Swelling index, Drug content, *in-vitro* drug release.

REVIEW OF THE LITERATURE:

1. **Hiba Sabah sabry and co-workers 2021** were formulated and evaluated levofloxacin and betamethasone ophthalmic high-water emulgel. They evaluated the physical properties such as gelling agent type, gelling agent concentration and emulsifying agent concentration and reported that formulation containing methyl cellulose as gelling agent showed promising results compared to other formulations, and the activity of levofloxacin was maintained in the combination. Commercial eye drops of betamethasone and levofloxacin release the drug over 1 h, and the recommended dosage regimen to be used is 2 drops up to 8 times a day. However, the high-water formulation of the same drugs release similar amount as eye drops over a period of 6 h based on the release studies, which potentially reduces instillation time to two or three times a day instead of eight times.
2. **Anroop B. Nair co-workers 2021** investigated and they formulated in-vivo evaluation of novel topical in-situ gel system to treat the ocular infection. It was found that gellan gum with sodium alginate substantially decreased the amount of gellan gum and contribute additional adhesive and gelling strength to the formulations. This novel ophthalmic in-situ gelling system is a feasible substitute to ophthalmic drops because of its inherent capacity to promote ocular bioavailability through sustained drug release, higher ocular permeability and prolonged residence time. They reported as the prepared gel was miscibility with the lachrymal fluids, convenience of instillation, minimized frequency of application and total dose of moxifloxacin can lead to better patient compliance.

3. **Sreevidya V.S. 2019** conducted a study on emulgels, to know the properties and how well they work when compared with other topical dosage forms like ointments and lotions etc. It was conducted to study spread ability, determination of pH, microbiological assay, physical appearance, theological study, drug content, accelerated stability study, globule size, centrifugation, in-vitro drug release, skin irritation, swelling index. They concluded that it is better for poorly water-soluble drugs or hydrophobic drugs in a water-soluble gel base.
4. **Prasanth VV and co-workers 2017** developed in-situ ocular gel of levofloxacin. LEV is a broad spectrum anti-bacterial agent, used in treatment of various ocular infections. In-situ ocular gels of LEV were prepared and in-vitro drug release indicated that it is potential drug delivery of LEV. It was concluded that the optimized formulations in combination of Sodium alginate and Benzalkonium chloride showed good antibacterial efficacy with non- irritant character. In- vivo studies are warranted to confirm these results in future.
5. **Ch. Pujitha and co-workers 2017** has studied about ophthalmic gel and they have formulated and characterized ofloxacin ophthalmic gels. Ophthalmic gels of ofloxacin were prepared by using the polymers HPMC K100, Carbopol and Sodium Alginate alone and in combination. Comparative drug release was estimated. Among all the formulations, the formulation having HPMC K100 and Carbopol at 0.5% each has shown a sustained release of drug for the estimated six hours of time. Finally, they have concluded that the combination of HPMC K100 and Carbopol was found to be optimized for ophthalmic gel of ofloxacin for a six-hour release.[5]
6. **Kalpesh Ashara and their co-workers 2017** conducted a study on type of materials that can be used in the formulation of Emulgels for their better action. They concluded that this is the best and useful topical dosage form, it can be used to load any kind of drug moiety especially for hydrophobic drugs and the side effects would be reduced.
7. **S.B. Makwana and V.A. Patel 2016** were formulated and evaluated characterization of in-situ gel for ophthalmic formulation containing ciprofloxacin HCI. Ciprofloxacin hydrochloride was successfully formulated as in-situ gel-forming eye drops using sodium alginate and HPMC. The results demonstrate that the alginate and HPMC mixture can be used as an in-situgelling vehicle to enhance ocular bioavailability and patient compliance. They have proved that (IG 3) was feasible alternative to conventional eye drops and ointment in terms of ease of administration with added benefits of sustained drug release which may ultimately result into improved patient compliance.
8. **Anand Panchakshri Gadad and co-workers 2016** formulated thermosensitive in-situ Gel for Ocular Delivery of Lomefloxacin. Thermoreversible sol gels are shear thinning systems which show temperature dependent gelation. Lomefloxacin HCI is a broad-spectrum antibiotic effective against gram positive and gram-negative bacteria. A combination of Pluronic F127 and Pluronic F68 along with sodium alginate was used to prepare the gel base. The rheological studies confirmed sol to gel transition at physiological eye temperature. They reported that pH of all formulations was in between 7 to 7.4. The drug content for all formulations was in between 95.55 to 98.18 %, which ensures dose uniformity in the formulation. They confirmed from the rheological studies that all formulation exhibited pseudoplastic rheology as evidence by decrease in viscosity with increasing in angular velocity and in-vitro drug release study indicated controlled drug release over a period of 8 hours.

9. **Yan Shen and co-workers 2015** performed a study on high-water for ocular delivery. In the coming years, topical drug delivery is expected to be extensively used for better patient compliance and tolerance and was formulated and evaluated Cyclosporin high water, since high-water is helpful in enhancing spread ability, adhesion, viscosity and extrusion. They concluded that polycarbophil-based high-water is able to extend the retention time on the ocular surface as well as improve the ocular bioavailability without any lesions.
10. **Snchal P. Mulye and co-workers 2013** formulated an emulgel using Indomethacin, they used two types of gelling agents, Carbopol 934 and xanthum gum. They evaluated various parameters like its appearance, pH, spread ability, viscosity, drug content and in-vivo drug release. The emulgel was optimized using a two-level factorial design. Influence of type of gelling agent was also investigated. Mathematical equations and response surface plots were used to relate the dependent and independent variables. The optimized formulations were then evaluated for anti-inflammatory, skin permeability, and stability for 3 months. This study shows Carbopol 934 when compared to xanthum gum formulations is less promising, hence, using the xanthum gum, a natural polymer is better than the synthetic polymer like Carbopol 934.
11. **Nagesh C and co-workers 2011** were performed a study on floating microspheres of Levofloxacin, which was prepared by a solvent evaporation method. The nature of polymer influenced the physical characteristics as well as floating behavior of the microspheres and they have concluded that the in-vitro buoyancy study confirmed the excellent floating properties of microspheres. The drug release was sufficiently sustained and non-Fickian transport of the drug from floating microspheres was confirmed. Hence, they have concluded that the floating microspheres of Levofloxacin prepared with HPMC and Eudragit- S 100 may provide a convenient dosage form for achieving best performance regarding flow, release and floating properties.
12. **Pamula Reddy Bhavanam and co-workers 2010** conducted a study on Levofloxacin using different types and concentrations of super disintegrants. Levofloxacin tablets containing different types and concentrations (5%, 10%) of super disintegrants (SSG, CCS and Cross povidone XL-10) were prepared by wet granulation method and subjected to disintegration and in-vitro drug release studies. The disintegration time for three formulations was observed.Lev 2 shows the better disintegration than the Levt and Lev 3. They concluded that levofloxacin oral formulation Lev 2(Cross povidone XL-10) with 5%, 10% shows the better disintegration time and % of drug release.
13. **Naseem A. et al., (2021)** formulated in situ ophthalmic gel of ciprofloxacin hydrochloride using HPMC (K15M) and Carbopol 940 and showed that its short half-life of elimination and polar characteristics, the bioavailability of ciprofloxacin hydrochloride was very low and it is thus necessary to apply the eye drops three times daily. To overcome this shortcoming, a controlled drug delivery system of ciprofloxacin hydrochloride was developed for the continuous release of the drug for 24 h. On the basis of in vitro, in vivo, and microbiological studies it was concluded that ciprofloxacin hydrochloride, a potent antibacterial agent, could

be successfully administered via a sol-to-gel system for the treatment of bacterial conjunctivitis.

14. **Raida S.et al., (2021)** formulated and evaluated ophthalmic controlled release in situ gelling systems for ciprofloxacin based on polymeric carriers. They have concluded that various controlled release in situ gelling systems for ciprofloxacin were designed and characterized in terms of ciprofloxacin release, mechanical, and mucoadhesive properties. Based on the results obtained from the in vitro characterization techniques, formulation containing carbopol,methyl cellulose in addition to ciprofloxacin was selected for microbiological evaluation. Theselected formulation offered compromise between optimal ciprofloxacin release and adhesiveness and rheological properties, and showed a prolonged antimicrobial effect againstgram-positive and gram-negative organisms.
15. **Mai Mansour et al., (2021)** formulated in situ forming hydrogel using Poloxamer407(P407) and Poloxamer 188(P188) HPMC or HEC and evaluated for in vitro drug release, sol-to-gel transition temperature and rheological behavior showed optimum release and improved ocular bioavailability when compared to marketed conventional eye drops.
16. **Sindhu Abraham et al., (2021)** formulated and evaluated an ophthalmic delivery system of an antibacterial agent ofloxacin based on the ion activated in situ gelation. They haveconcluded that Ofloxacin, a broad-spectrum antibacterial agent used in the treatment of ocularinfections was successfully formulated as an ion- activated in situ gel forming ophthalmic solution using sodium alginate in combination with HPC as a viscosity enhancer which sustained the drug release over a period of 8 hours. The polymers used are inexpensive and easily available. The formulation also promises to reduce the frequency of drug administration,thus improving patient compliance. As the concept involved is novel and the methodology used for the preparation is simple as that of conventional ophthalmic liquid dosage form, it is industrially oriented and economical.
17. **Jagadish Balasubramanian et al., (2021)** formulated and evaluated In vitro and in vivo evaluation of the Gelrite® gellan gum-based ocular delivery system for indomethacin. They have concluded that Indomethacin was successfully formulated as an in-situ gelling system using gellan. The formulated systems provided sustained release of the drug over an 8-hour period in vitro and the developed formulations were devoid of any deleterious effect on the ocular tissues. The formulations demonstrated better therapeutic efficacy compared to the standard suspension because they were successful in improving the clinical parameters monitored for prolonged periods (24 hours). Hence, this can be viewed as a viable alternative to conventional eye drops by virtue of its ability to enhance pre-corneal residence time and thereby ocular bioavailability. The ease of administration coupled with its ability to provide sustained release could probably result in less frequent administration, thus enhancing patient compliance.
18. **Doijad R.C, et al., (2021)** formulated an ophthalmic drug delivery system of an antibacterial agent gatifloxacin, based on the concept of ion activated system. Sodium alginate was used in combination with HPMC (E50LV) and showed therapeutically efficacious, stable, non-irritant formulations and provided sustained release of the drug over an 8-hour period.[21]
19. **Sathish Kumar P. Jain, et al., (2021)** formulated and evaluated ophthalmic delivery system for ciprofloxacin hydrochloride. They have concluded that the concept of pH-triggered in situ gelation by using poly (acrylic acid)(Carbopol 980NF) as a phase transition polymer and

HPMC(k100LV) as release retardant and reported the formulation was stable and non-irritant to rabbit eyes and showed sustained in vitro release.

20. **Ega Chanra Mohan et al., (2020)** formulated and evaluated in-situ gels for ocular drug delivery. They have concluded that Ciprofloxacin Hcl, a broad spectrum antibacterial against in the treatment of ocular infections, was successfully formulated as pH-triggered in-situ gel forming eye drops (0.3% w/v) using carbopol 940 and methocel E50LV, temperature dependent in-situ gel forming eyedrops (0.3% w/v) using pluronic F-127 and methocel E50LV and ion activated in-situ gel forming eye drops (0.3% w/v) using gelrite as gelling agent. The formulations were liquid at the formulated pH use between of (6.4 to 7.1) and underwent rapid gelation up on raising the pH (7.4) and temperature (37 C). The developed formulation was therapeutically efficacious, stable, non-irritant and provided sustained release of the drug over a 6 hours period, but Gelrite formulation showing long duration of release followed by combination of carbopol, HPMC and pluronic F-127 & HPMC.
21. **Sivanaga S. et al., (2019)** designed and evaluated novel fast forming pilocarpine- loaded ocular hydrogels for sustained pharmacological response. They have concluded that resistance to external forces, give high pilocarpine loading, and provide sustained pilocarpine release. These hydrogel formulations are administered into the eye as a solution, rapidly forming a hydrogel that is able to withstand the shear forces in the cul-de-sac of the eye. The in vivo results show that compared to drops, the hydrogel formulations provide prolonged pharmacological response as measured by a decrease in pupil diameter with no visible irritation. Overall, the results support the rationale behind using PEG-based hydrogels as ocular drug delivery systems.

CONCLUSION:

The formulation and assessment of levofloxacin ocular emulgel present a promising approach to improve the treatment of bacterial infections of the eye. Emulgels, with their double release systemcombining gel and emulsion, offer a convenient and accessible delivery system. By incorporating polymers such as sodium alginate, xanthan gum, and methyl cellulose, the emulgel can achieve extended resident duration in ocular tissues, decrease instillation time, and improve patient compliance.The ocular emulgel formulation shows several advantages over traditional topical treatments like creams and ointments. It enhances drug absorption through the skin, bypassing first-pass metabolism and offering localized therapeutic effects. Additionally, emulgels provide better spreading constants, improved stratum corneum penetration, and enhanced drug solubility,resulting in optimized pharmacologic activity with lower dosage requirements.

Levofloxacin, a broad-spectrum antibacterial drug belonging to the quinolone antibiotics class, is well-suited for ocular emulgel formulations. The emulgel not only prolongs the drug's residence time in the eye but also reduces the risk of bacterial infection. The evaluation of various parameterssuch as pH, spreadability, swelling index, viscosity, drug content, centrifugation, antibacterial activity, in-vitro drug release, and stability further ensures the effectiveness and reliability of the developed ocular emulgel.

Overall, levofloxacin ocular emulgel holds great potential as an innovative and efficient method for delivering antibacterial activity in the treatment of bacterial eye infections. Further

research and studies are warranted to validate its effectiveness in clinical settings and explore its potentialapplications in ocular therapeutics.

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