International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Issue 5, 2022

Review Article

A REVIEW ON HOW TO CHARACTERIZE AND EVALUATE THE OPHTHALMIC *IN SITU* GEL PREPARATIONS

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Received: 18 May 2022, Revised and Accepted: 22 Jun 2022

ABSTRACT

In situ gelling systems are becoming one of the most popular and well-known, with many potential benefits from delivery systems, such as ease of use and ease of manufacture, improve adherence and patient comfort by minimizing the frequency of drug administration. In this review, we will describe the characterization and evaluation of the ophthalmic in situ gel preparation. Among them are physical evaluation (appearance and clarity, pH, isotonicity, gelation temperature, gelling capacity, viscosity, and stability), chemical evaluation (determining drug content, drug release), microbiological evaluation (sterility, ocular irritability, ocular tolerability, antimicrobial activity, hemolysis activity, bovine corneal opacity and permeability (BCOP) test, preservative efficacy test (PET), microtetrazolium (MTT) reduction cytotoxicity test), and *in vivo* evaluation such as pharmacokinetic and pharmacodynamic evaluation. Characterizing the chemical, physical, microbiological, and miscellaneous properties of ophthalmic in situ gel formulations can meet the ideal requirements and help determine the best formulation of ophthalmic in situ gel to achieve higher bioavailability values, longer contact times, minimize side effects, not causing irritation or liquid tear production, and providing a maximum therapeutic effect. In situ gels offer the primary requirement of a successful controlled release product that is increasing patient compliance.

Keywords: *In situ* gel, Controlled release, Isotonicity, Gelation temperature, Gelling capacity, Ocular irritability, Ocular tolerability, Hemolysis activity, Bovine corneal opacity, Permeability test, Preservative efficacy test

DOI: https://dx.doi.org/10.22159/ijap.2022v14i5.45248. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Penetrating the eye's protective barriers without suffering serious tissue injury is a significant challenge [1], since eye has a highly impervious organ to foreign substances from environmental such as exposure to tobacco smoke, allergens, contact lens wear, exposure to TV or computer and so on [2]. The important concern in ocular drug delivery is achieving adequate therapeutic efficacy at the site of action, which might be hampered primarily by aqueous humor loss, which consequences in only a small percentage of the drug could be absorbed ocularly [3]. The requirements of drug candidates consist of no irritation or side effects, no dose more than 25 mg, no toxic metabolites, no offensive odors, adequate absorption property, and suitability in terms of stability [4].

The '*in situ* gel' method has emerged as one of the excellent progressive drug delivery systems. Its particular function characteristic of 'sol to gel' transformation aids within side the continuous and controlled release of drugs, in addition to improved affected user compliance and comfort with eliminating the need for frequent intraperitoneal injections for the treatment of posterior eye conditions [5, 6].

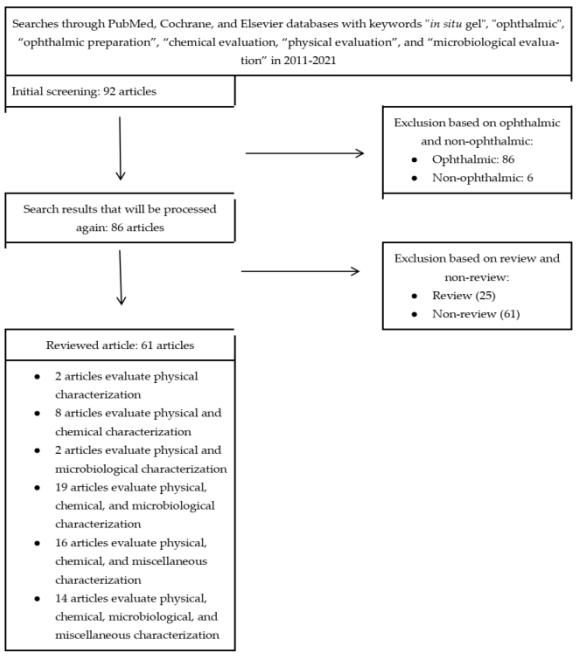

Fig. 1: PRISMA 2020 flow diagram for literature search design and process

A formulation which is in a liquid (solution) form before prior to entering the body change to gel form under different physiological conditions is referred to as an in situ gelling method. Some materials or excipients used in the in situ gel are based on several mechanism triggered by temperature (such as pluronics, polymethacrylates, and tetronics), pH shift (such as carbopol and cellulose acetate phthalate), solvent exchange (such as gelrite and sodium alginate), UV radiation, and the presence of particular molecules or ions all influence the sol to gel transition. Drug delivery systems with the above-mentioned 'sol to gel' transformation properties may be extensively used for bioactive molecule sustained delivery vehicle preparation [1, 5].

In environmentally sensitive polymer systems, the most commonly used stimulus in the in situ gelling formulation is temperature. The temperature shift is often able to control that can be used *in vitro* and *in vivo* studies. On this system, gelation will be triggered by body temperature and no external heat is needed. These hydrogels seem to be liquid at 20-25 °C (room temperature) but gel due to body fluids at 35-37 °C. This system employs thermoresponsive or temperature-sensitive polymers, which exhibit a rapid and discontinuous change in physical properties as a function of temperature. At high or low temperatures, these polymers show a miscibility distance, indicating that an upper or lower critical solution temperature exists [5]. The advantages of thermosensitive gels over aqueous drops include sustained drug release, prolonged drug contact time with the cornea, fewer applications, fewer side effects, and higher bioavailability [7].

The aim of this review article is to clarify every aspect of in situ gels in a way that draws the reader's attention to a particular feature while also contributing to research and development.

METHOD

In this study, researchers used literature data collection with PRISMA 2020 flow diagram as follows

RESULTS AND DISCUSSION

The main requirements of an in situ gel-forming system are viscosity and gel-forming capacity In this review; we will discuss characterization and evaluation of in situ gel preparations to ensure that a drug or preparation meets the requirements and can be used safely, proves to be a viable alternative to conventional eye drops and ointments, with the added benefit of sustained release of the active ingredient, which ultimately leads to improved patient compliance. The characterization and evaluation were reviewed on physicochemical, physical, and microbiological aspects. The physicochemical aspects include drug content, drug release, and drug interactions with polymers, and the physical aspects include appearance and clarity, pH, isotonicity, gelation temperature, gelling capacity, viscosity and stability. As for the microbiological aspect, it includes sterility, ocular irritability, ocular tolerability, antimicrobial activity, hemolysis activity, bovine corneal opacity and permeability (BCOP), MTT reduction cytotoxicity, and preservative efficacy test (PET). In addition, it will also be presented about pharmacokinetics and pharmacodynamic characterization. In the followings, we present the procedures for characterizing and evaluating of ophthalmic in situ gel preparations in terms of various aspects.

Physicochemical

Drug content

Evaluation methods to determine the drugs content can be done using:

UV-VIS spectrophotometry

In situ eye drops or gel dosage to be determined is taken 1 ml and then diluted to 100 ml. After that, 5 ml of aliquot was taken and then diluted again. Then the sample levels were measured using UV-Vis spectrophotometry according to the wavelength of the tested preparation [8-11]. The active substances in this review that employ the UV-Vis spectrophotometry method are chloramphenicol, ciproploxacin, dorzolamide, dorzolamide HCl, levofloxacin, acyclovir, balofloxacin, betaxolol HCl, moxifloxacin, naproxen, ofloxacin, pefloxacin mesylate, prednisolone sodium phosphate, sodium alginate, and voriconazole.

High-performance liquid chromatography (HPLC)

The HPLC used is Reversed-Phase HPLC; the method is to compare the *in vitro* drug release profile of drug formulations developed with drug formulations on the market [12]. The active substances in this review that employ the HPLC method are brimonidine tartrate, brinzolamide, and octreotide.

Drug release

Evaluation method of drug release can be done using:

Franz cell diffusion

The use of Franz diffusion cells for *in vitro* release studies was carried out by adjusting the stirring rate and the temperature was set at 50 rpm and 37±0.5 °C. Then 200 µl aliquot of the formulation was added to the cornea and blended with 56 µl artificial tears fluid. At certain time intervals, for example after 0.25; 0.5; 1; 2; 4; 6; 8; 12; and 24 h of centrifugation (4,000 rpm speed was used) at a sample of 0.2 ml and extracted for 5 min before being analyzed by HPLC [13]. The active substances in this review that employ the Franz cell diffusion method are brimonidine tartrate, chloramphenicol, dexamethasone sodium phosphate and tobramycin sulphate, ketotifen fumarate, moxifloxacin (carbopol in situ gel), ofloxacin, and prednisolone sodium phosphate.

USP dissolution

In vitro drug release preparations were tested using a modified USP apparatus II paddle method and simulated tears fluid (STF) (pH 7.4) as the dissolution medium. Used a glass cylinder with a diameter of 2.5 cm (both ends are opened), take a dry dialysis membrane that has been previously soaked in STF (pH 7.4) and tie it to one end of the cylin glass. 1 ml of the formulation is inserted into the dialysis membrane. The glass cylinder is attached to the USP II equipment shaft. Suspend the cylinder with 50 ml of the dissolved medium at 34±0.5 °C until the membrane does not touch the media. Set the shaft speed to 50 rpm at 1, 2, 3, 4, 5 and 6 h; aliquots were replaced with the same volume of dissolution medium. STF (pH 7.4) was used to dilute the aliquot; after that, it was analyzed by UV spectrophotometer 322 nm [1]. The active substances in this review that employ the USP dissolution method are chloramphenicol, ciprofloxacin, pefloxacin mesylate, and sodium alginate.

Dialysis

Dialysis tubes used to determine drug release *in vitro* have a molecular weight limit of 8,000-14,000. 2 ml of the formulation were taken, then placed into the dialysis tube. Add 50 ml of STF at a storage temperature of 34.5 °C or with a phosphate buffer solution (pH 7.4) stored at 37 °C into a vibrating water bath. In this experiment, the sink condition must be kept constant. At appropriate intervals (0.17, 0.5, 1, 2, 4, 6, 8, 12, 24, 48, 60, 72, 96, 108, 120, 132, and 144 h), the release medium (4 ml) was withdrawn and replaced with 4 ml of fresh medium [14,15]. The amount of drug released from the in situ gel was measured with a spectrophotometer set to its maximum wavelength [15]. The active substances in this review that employ the dialysis method are Cur-BSA-NPs-Gel and voriconazole.

Drug-polymer interactions

Evaluation method of drug-polymer interactions can be done using:

Fourier transform infrared (FTIR)

The 2 mg sample was dispersed in 200 mg KBr [16], before being compressed into pellets, the preparation must be ground with a mortar-pestle. The pellets are placed in the light path, 2 cm^{-1} resolution at a frequency of 4000 to 400 cm^{-1} is the spectrum that will be captured by the instrument. The spectrum generated by KBr is used as a blank [17].

Differential scanning calorimetry (DSC)

DSC is used to determine whether a chemical substance has changed in the thermogram, polymer-drug interaction studies and thermal

analysis were compared with the pure active ingredient used for gelation [18]. 2-4 mg of the sample is put in an aluminum pan then heated and flowed with nitrogen (20 ml/min) at a scanning speed of 100 c/min from 25 to 340 °C. The standard used is an empty aluminum pan [17].

X-ray diffractometer (XRDP)

An X-ray diffractometer was used to monitor the powder XRD patterns of the sample powder and physical mixture formulation with copper as the X-ray target [16]. The diffractograms were recorded in the following conditions: volt 45 kV, current 30 mA, and room temperature. The scattering angle (2θ), which ranged from 10 to 90 °, was used to collect the data [19].

Appearance and clarity

The formulation was observed visually for the color and the clarity in black and white background with a fluorescent lamp [20] or under good light [21].

pH

pH in the formulation was measured with a pH meter. Previously, buffer solutions with pH 4 and 7 were used to calibrate the pH meter. The expected pH range for in situ gel formulations is 5-7.4 [22, 23].

Isotonicity

The formulation is blended with a few drops of blood and compared to standard ophthalmic preparations under a microscope with ×45 magnifications [24, 25]. Isotonicity must be maintained in all ophthalmic preparations to avoid tissue damage and eye irritation [26]. The blood cells will remain intact in the isotonic solution. Meanwhile, when the solution becomes hypertonic, the cells will experience shrinkage and will swell when the solution is hypotonic [24].

Gelation temperature

The gelation temperature was determined by immersing a test tube containing sample solution in a water bath where the temperature was preserved at 37±5 °C for 2 min. The temperature is increased slowly and observed by placing a thermometer in a test tube. Record the temperature as T1 when the gel is formed i.e. when there is no formulation flow. The heating of the gel further causes the gel to melt and form a viscous liquid and begin to flow; this temperature is recorded as T2, which is the melting temperature of the gel. The mean of the two temperatures was calculated as the critical gelation temperature [17, 22].

Gelling capacity

Procedure 1

This is done by adding a drop of the freshly prepared sample into 2 ml of STF in a bottle. Then observed and recorded the time it takes for the 'gel' to form or 'gel' to dissolve in 7.4 pH phosphate buffer, the time can be used to determine the appropriate polymer concentrations or gelling agent to form in situ gelling systems [3].

Procedure 2

They used water-soluble dyes like amaranth, Congo red, indigo blue, and others, which they combined with the in situ gel after dissolving 1 g in distilled water. The gelling capacities of the formulations were measured *in vitro* by placing 5 ml of gelation solution (STF) in a glass test tube and keeping the temperature constant at 37±0.5 °C. It quickly turned into a stiff gel-like substance. Gelling capacities are measured *in vitro* by the gel rigidity along with the time it took for the formulation to transform into a dense gel remains the same. Furthermore, the color was applied to give the gel a visual appearance [27].

Some researchers interpret gelling capacity differently, such as (-) No gelation; (+) Gels after some min and breaks up quickly; (++) Gelation immediately then lasts for several h; (+++) Gelation immediately thereafter remains for an extended period; (++++) Stiff gel in studies [12,20,25,28,29], or (+) gel is shaped in>40 s and melts in 1–2 min; (++) Gel is shaped in 30–40 s, melts in 2–5 min; (+++) Gel is shaped in<30 s and melts in>5 min [23], or (+) No gelation; (++) Gelation occurs after several min with a flowing gel-like liquid; (+++) Gelation immediately with the formation of an easy-flowing gel with good consistency; (++++) Non-flowing, consistent, and thick in [30].

Viscosity

Viscosity is one of the main factors in determining the length of stay of the drug [31]. The viscosity of the formulation is determined at different shear speeds and temperatures using a viscometer such as a Brookfield viscometer [29, 32], a Rion viscometer [23], and an NDJ-5S viscometer [21] or using a rheometer [33].

Stability

The formulations can be stored in different conditions, such as refrigerated condition, room temperature and stress condition, i.e. high temperature, then evaluated in several parameters such as appearance and clarity, pH, viscosity, gelation capacity, drug content, or other parameters. The retention period varied across studies, such as at regular intervals for a period of 28 d [20], 35 d [34], 90 d [15], or 180 d [19, 33], with a certain evaluation interval.

Microbiological

Sterility

The sterility of the prepared formulations was tested using the direct inoculation method aseptically under ultraviolet radiation [35]. Three sets of agar medium were used, the first being a negative control containing sterile media, the second being a positive control for this sterilized media inoculated with Staphylococcus aureus, and the third being a test [36]. Using a sterile pipette, 2 ml of the test solution was withdrawn and transmitted to each 20 ml medium separately. The temperature used to incubate the thioglycolate liquid medium was 30-35 °C and 20-25 °C was used to incubate soybean casein for a minimum of 14 d [29].

Ocular irritability

Three white albino New Zealand rabbits (1.5-2 kg, 13 w old) were used in the Draize test. In this test, approximately 100 µl was placed in the rabbit's right eye's lower cul-de-sac twice a day; normal blinking was permitted, though the eyelids could be held together for several seconds after instillation [24, 37]. As a control, the left eye was treated. Redness, swelling, and watering of the eyes in rabbits were stated at 1 h, 24 h, 48 h, and 72 h after instillation [37]. These criterias were derived from each rabbit eyes (cornea, iris, and conjunctiva) weighted score, as well as the sum of these scores [22]:

Table 1: Draize total score

Classification	Maximal average draize total score (MAS)
Non-irritant	0-≤0.5
Slight irritant	0.6-≤15
Mild irritant	16-≤25
Moderate irritant	26-≤50
Severe irritant	>50

Ocular tolerability

The ocular tolerability is evaluated using a modified Hen's Egg Test Chorioallantoic Membrane (HET-CAM) test. Eggs (50-60 g) were chosen and grouped into three groups, each group containing three eggs. Incubation was carried out (temperature 37±0.5 °C) in an incubator that had been moistened for all eggs for 3 d. After every 12 h, the trays containing eggs were gently rotated. Using sterile techniques, egg albumin was extracted from the egg's pointed end as much as 3 ml on the third day. With the help of a heated spatula, 70 % alcohol-sterilized Parafilm was used to seal the hole. An equatorial position was retained to keep the chorioallantoic membrane (CAM) of eggs from evolving elsewhere in the shell.

On the fifth day of incubation, the eggs were candled, and non-viable embryos were taken out every day thereafter. About 0.5 ml of the formulation was implanted directly onto the CAM surface via a 2 cm x 2 cm window cut at the egg equator on the tenth day, then left in contact for 5 min. Vascular damage which could indicate hemorrhage, hyperemia, or coagulation was examined through the membrane [38]. A positive control with strong irritant effect was 0.5 M NaOH, while propylene glycol caused mild irritant, and a negative control was normal saline. The test's mean score enabled evaluation using a Draize test similar classifier [38, 39]:

Table 2: The test's mean score enabled evaluation using a draize

Cumulative score	Appearance	Classification
≤0.9	No visible haemorrhage	Non-irritant
1-4.9	Only visible membrane discoloration	Mild irritant
5-8.9	Haemorrhage	Moderate irritant
9-21	Structure completely covered by membrane discoloration or haemorrhage	Severe irritant

Antimicrobial activity

Antimicrobial activity was determined using the Cup plate technique conducted in a laminar air flow. As a control, a standard sample of pure drug and test solution of the formulation in concentrations of 1, 1.5, and 2 g/ml with developed formulations (10 g/ml) at pH 7.4 were prepared. Plates were inoculated with 0.3 ml of *Staphylococcus aureus* and *E. coli* [40] or *Pseudomonas aeruginosa* [29] cultures, or even *Candida albicans* organisms [15]. After the media solidified, wells were punched with a sterile borer, standard and test solutions were added, and the wells were incubated for 24 h at 37 °C. Each well's zone of inhibition was measured and contrasted to the standard zone of inhibition. The whole experiment was conducted in a laminar air flow chamber [40].

Hemolysis activity

Ethylenediaminetetraacetic acid (EDTA) was used as an anticoagulant 5 ml to healthy individual's whole blood. For 20 min, blood was centrifuged at 1500 x g. After removing the buffy coat, the packed cells (RBCs) were washed three times with normal saline. Normal saline was added to the cells to achieve a 40–50 % of hematocrit. In two separate test tubes, positive and negative controls were prepared by diluting 100 µl of RBC to 3 ml with double distilled water and normal saline, respectively. RBC will be lysed in the positive control, but not in the negative control. In test tubes, formulations were incubated at 37 °C for one hour with 100 µl RBCs before being diluted to 3 ml with normal saline. After centrifuging the blood samples for 20 min at 795 x g, the supernatant's absorbance was determined using a UV spectrometer at 540 nm. The percentage of hemolysis was calculated using following formula [41]:

$$\% \text{ Hemolysis} = \frac{\text{Absorbance of sample}}{\text{Absorbance of 100\% haemolysis}} \text{ x } 100$$

Bovine corneal opacity and permeability (BCOP) test

For validation purposes, three different controls were used: 0.5 M NaOH was used as a positive control which had a strong irritant effect. Mild irritation was caused by giving propylene glycol and normal salt as the negative control. Tiny plastic cups could be used to retain the cornea upwards, that was then located in a moist environment of a 37±0.5 °C closed water bath for 10 min. To characterize and localize the instillation site and to achieve test material application efficiency and reproducibility, a silicone O-ring (1.78 mm of thickness and 7.6 mm of internal diameter) was carefully located on the cornea's central part. Add one drop of saline solution to the silicon O-ring and then balance the eyes for 5 min in a closed water bath. The volume of the sample substance used on the cornea was 0.1 ml. Upon 30 s, the eyes were washed with 10 ml saline before spending another 10 min in the closed water bath. The severity of the corneal injury was then assessed visually, followed by the instillation of a 2 % w/v sodium fluoresce in solution at pH 7.4 to assess corneal epithelium integrity. The fluorescence was detailed by utilizing an appraisal light with such a cobalt blue channel. The analyses were specific individual scores for opacity, corneal epithelium integrity (staining degree), and corneal epithelium separation. The sum of light which transmits through the cornea characterizes corneal opacity, though the sum of fluoresce in color which moves through the corneal stroma characterizes corneal permeability. Then the total score was determined, and the mean scores of each three treated eyes were used to define the corneal irritation potential of the tested formulations [39].

MTT reduction cytotoxicity test

Mosmann's procedure was used to analyse function of mitochondrial and viability of cells in corneal epithelium during the MTT cytotoxicity test. Into 96 well plates, primary human corneal epithelium were treated in corneal epithelial cell basal medium and cultivated at approximately 2 x 104 cells/well. At its final concentration, the medium consist of several supplements such as 5 mg/ml of Apotransferrin, 1 ml of proprietary formulation CE Growth Factor, 1.0 mmol of epinephrine, 0.4 % of extract P, 100 ng/ml of hydrocortisone hemisuccinate, 6 mmol of L-glutamine, and 5 mg/ml of recombinant human insulin. Prior to treatment, cells in the 96-well culture plate were permitted to establish for 48 h. Following that, 4 wells media was substituted with new media containing treatments per condition. The treatments included plain and loaded in situ gel formulations with 5 mg/ml drug. Aseptically, the entire solution is prepared and the formulation was available at the culture medium. The negative control was untreated media, while the positive controls were 100 mg/ml hydrogen peroxide and 0.01 % w/v benzalkonium chloride. The medium was pumped gently and cells were rinsed twice using sterile phosphate buffer saline (PBS) at 37 °C at 4 and 24 h since the treatment and cells were incubated at 37 °C with the medium being 0.5 mg/ml 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) with a volume of 200 µl per well for 4 h. Each well was rinsed again using sterile PBS and then each well was added with 200 µl of dimethyl sulfoxide (DMSO) which was intended to lyse cells. Careful cell agitation was performed to achieve a homogeneous lysate before analysis at 540 nm in a plate reader. Experiments were carried out in three replicates, and mean scores were computed. The findings were given as a percent of the control cultures [39].

Preservative efficacy test (PET)

Soya bean casein digest agar medium was used to culture *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, while sabouraud glucose agar medium was used to culture *Aspergillus niger* and *Candida albicans*. Both organism cultures were diluted aseptically to achieve 10-6 CFU/ml with sterile WFI. About 5 test tubes which contained 10 ml eye drops and 0.1% cultures, were used to transfer all of the cultures. The first counts were taken. Bacteria were incubated at 32.5±2.5 °C, while fungi were incubated at 22.5±2.5 °C. On the 7th, 14th, and 28th d, the number of microorganism colonies was counted and the acceptable range for preservative effectiveness was checked [17].

Pharmacokinetics characterization

Pharmacokinetics study was carried out using male albino rabbits (2–3 kg, New Zealand breed) as much as four. Two of four applied conventionally marketed eye drops, while the rest applied developed formulations. Using a micropipette, about 1 drop developed formulation or 40 µl marketed eye drop as instilled into the lower cul-de-sac. Disposable glass capillaries were used to

collect tear fluid samples of the lower border tear strip after washing the eyes with 0.5 ml simulated tear fluid at 15, 30, 60, 90, 120, and 180 min. HPLC method was used to analyze samples after further dilution [17]. The concentrations of drug in tear fluid were determined using a trapezoidal method to determine the area under the curve, AUC(0-∞) in g. h/ml. Actual data points were used to calculate the aqueous humor's maximum concentration Cmax (g/ml) and the time required to achieve Tmax (h) [42]. The remaining pharmacokinetic parameters were computed using a non-compartmental pharmacokinetic model and Excel software [17].

Pharmacodynamic characterization

Intraperitoneal injection was performed into male Wistar rats (220±20 g) using 100 µg Egg Albumin (EA)±20 mg alum in 1 ml PBS (pH 7.4). After 14 d, rats were given 10 % EA in PBS as much as 10 µl topically. Around 15 min before topical administration, each eye was applied with 1 mol/l of dl-dithiothreitol with a mucolytic agent in fresh PBS of 20 µl to achieve an impressive ocular reaction. EB or Evans Blue (2 mg/100 g) mixed with 1 ml PBS was given prior to intravenous testing. Chlorine hydrate at a concentration of 5 % (0.2 ml/100 g) was used to anesthetize the animal intraperitoneally [13].

There were 30 animals in each of the two groups (gels and solutions). About one drop of 0.1 % formulation administered to one eye of each animal, while the other eye was left untreated as a control. About 1 h after the challenge, all rats were exsanguinated. Globes and adnexa were measured at 5, 10, 15, 30, 45 min after administration. After that, the tissue was removed, measured, and immersed in a 5 ml extraction solution (sodium sulfate 0.5 %+3: 7 v/v acetone), stirred vigorously and needed to be stored at 20-25 °C (room temperature). The solutions were separated by centrifugation at 1,000 rpm for 10 min after 24 h. At 620 nm, the color intensity of the supernatant was measured using spectrophotometry. The absorbance unit was converted to micrograms of EB per milliliter of solution using a standard curve, and extravasation of EB in eye tissue was calculated. Drug efficacy can be calculated by looking at the percentage inhibition of the eye response in the treated eye.

$$\% \text{ IR} = \frac{\text{UCE} - \text{DTE}}{\text{UCE}}$$

Where IR represents the rate of drug inhibitory, DTE represents the EB content in the drug-treated eye, while UCE represents the EB content in the untreated control eye [13, 43].

CONCLUSION

In situ ophthalmic gel is a gel preparation that begins as an ophthalmic solution dripped into the eye and then transforms into a gel upon contact with the eye's surface. Characterizing the chemical, physical, microbiological, and miscellaneous properties of ophthalmic in situ gel formulations containing various active substances such as chemical evaluations (drug content using UV-Vis spectrophotometry and HPLC methods, drug release using Franz cell diffusion, USP dissolution, and dialysis methods; and drug-polymer interactions using FTIR, DSC, and XRDP methods), physical evaluations (appearance and clarity, pH, isotonicity, gelation temperature, gelling capacity, viscosity, and stability), microbiological evaluations (sterility, skin irritability, ocular irritability, ocular tolerability, antimicrobial activity, hemolysis activity, BOCP test, PET, and MTT reduction cytotoxicity test), and miscellaneous evaluation (pharmacokinetics and pharmacodynamics) can meet the ideal requirements and help determine the best formulation of ophthalmic in situ gel to achieve higher bioavailability values, longer contact times, minimize side effects, not causing irritation or liquid tear production, and providing maximum therapeutic effect.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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