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Tacrolimus-Loaded Solid Lipid Nanoparticle In Situ Gel: A Novel Strategy for Ocular Delivery in Immune Conjunctivitis

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ABSTRACT

Effective ocular delivery of tacrolimus remains challenging due to rapid clearance and low bioavailability. This study aimed to design an in situ gel incorporating tacrolimus-loaded solid lipid nanoparticles (TAC-SLNs) for improved therapeutic outcomes in immune conjunctivitis. The TAC-SLNs in situ gel was optimized and evaluated for particle morphology, size, surface charge, drug encapsulation efficiency, loading capacity, and release profile in vitro. Pharmacokinetic and pharmacodynamic studies were also performed in animal models to assess ocular retention and treatment efficacy. The TAC-SLNs in situ gel was prepared via homogenization followed by probe sonication, yielding nanoparticles with an average diameter of 122.3 ± 4.3 nm. Gelation did not significantly affect particle size. Rheological testing indicated pseudoplastic flow behavior, with viscosity increasing with temperature and forming a stable gel at 32°C. Drug release studies demonstrated sustained delivery both in vitro and in vivo. Animal experiments revealed enhanced pharmacodynamic performance of the in situ gel compared to TAC-SLNs alone or conventional eye drops, showing improved efficacy in reducing conjunctival inflammation. TAC-SLNs in situ gel offers a promising approach for ocular tacrolimus delivery, combining prolonged retention, controlled release, and enhanced therapeutic effect, highlighting its potential for managing immune conjunctivitis.

Keywords: Tacrolimus, Ocular delivery, In situ gel, Solid lipid nanoparticles

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Introduction

Immune-mediated inflammatory diseases affecting the anterior segment of the eye (IIAODs), such as conjunctivitis and anterior uveitis, are common ocular disorders that can lead to severe complications and are significant contributors to vision impairment [1]. Conjunctivitis is typically treated with antibiotic eye drops for 5–7 days, often requiring frequent dosing (e.g., twice daily), which can result in poor patient adherence due to the inconvenience of repeated administration. The eye's protective mechanisms, including blinking and tear turnover, limit drug absorption and shorten the therapeutic effect. Studies indicate that tear drainage and blinking can reduce the drug concentration in the eye by up to tenfold within 4–20 minutes [1].

To improve therapeutic efficacy, strategies that extend the precorneal residence time of ocular drugs are essential. Various novel drug delivery systems, such as liposomes, nanoparticles, and nanocapsules, have been developed to slow drug clearance and increase retention on the ocular surface [2–8].

Tacrolimus (TAC), a macrolide immunosuppressant, is widely used in managing conjunctivitis and other immune-mediated eye diseases. However, TAC is highly lipophilic and poorly soluble in water (1–2 µg/mL), which limits its therapeutic application [9–13]. Conventional eye drops require frequent administration or high concentrations due to rapid precorneal drainage, often resulting in fluctuating drug levels. TAC also undergoes hydrolysis in aqueous solutions, further reducing stability [14]. Commercial eye drops generally contain mostly undissolved TAC, but drugs like TAC ideally need to be in a dissolved form to reach target tissues and exert therapeutic effects

[15]. Dissolved TAC is expected to penetrate ocular tissues more efficiently, improving bioavailability and reducing the risk of treatment failure [15].

Given these challenges, there is a clear need for advanced ocular drug delivery systems that consider both physiological barriers and the physicochemical properties of the drug. In situ gels have emerged as a promising approach due to their reversible sol-to-gel phase transitions and pseudoplastic behavior, which minimize drug loss from blinking [16]. Administered as liquid drops, in situ gels transform into a gel upon contact with the eye, increasing precorneal retention and enhancing drug absorption.

Solid lipid nanoparticles (SLNs) have also gained attention as ocular delivery vehicles, particularly for lipophilic drugs. Their primary advantage lies in their ability to encapsulate hydrophobic molecules within a lipid matrix, improving solubility and permeability [17, 18]. SLNs have been successfully applied for ocular delivery of drugs such as natamycin [19], triamcinolone [20], indomethacin [21], and atorvastatin [22], showing advantages over conventional formulations like solutions and suspensions. However, the combination of TAC-loaded SLNs with in situ gel (TAC-SLNs-ISG) remains largely unexplored in ocular therapy.

The present study aimed to develop a combined ocular delivery system of TAC using SLNs and in situ gel, and to compare it with conventional eye drops and SLNs alone. The optimized formulation was evaluated for particle size, surface morphology, zeta potential, encapsulation efficiency, drug loading, and in vitro release characteristics. Additionally, in vivo pharmacodynamic performance was assessed.

Materials and Methods

Materials

Tacrolimus (TAC) was obtained from Kerui Pharmaceutical Co., Ltd. (Fujian, China). Glyceryl behenate (Compritol® 888 ATO) and glyceryl monostearate (GMS) were purchased from Gattefossé. Pluronic® F-68 (Poloxamer 188), Pluronic® F-127 (Poloxamer 407), and Tween® 80 were supplied by Sinopharm Chemical Reagent (Shanghai, China). All other chemicals were of analytical grade and used as received without further purification.

Preparation of TAC SLNs-ISG

TAC-loaded SLNs in situ gel was prepared using a combination of homogenization and probe sonication [23]. Briefly, Compritol® 888 ATO (0.25% w/v) and GMS (2% w/v) were dissolved in 2 mL dichloromethane and heated to 80°C. TAC (0.1% w/v) was added under continuous stirring to form a homogeneous drug-lipid phase. The organic solvent was removed under vacuum at 45°C to create a lipid film, which was further dried at 37°C to eliminate residual solvent. Simultaneously, an aqueous solution of Tween-80 (0.5% w/v) and glycerin (2% w/v) was heated to 30°C and gradually added to the molten lipid mixture under constant stirring to produce a pre-mixture. This mixture was sonicated in an ice bath for 10 cycles using a probe-type ultrasonicator (S220, Covaris, USA) to form TAC-SLNs. Finally, TAC-SLNs were combined with a solution of Poloxamer 188 (12% w/v) and Poloxamer 407 (26% w/v) under ice bath conditions to obtain the TAC-SLNs-ISG formulation.

Characterization of the system

Particle size and zeta potential

The mean particle size, polydispersity index (PDI), and zeta potential of TAC-SLNs-ISG were measured using a Zetasizer NanoZS (Malvern Instruments Ltd.) at 25°C. Measurements were conducted in automatic mode. The hydrodynamic diameter was calculated from the autocorrelation function of scattered light intensity, assuming spherical particle geometry.

Entrapment efficiency

The entrapment efficiency (% EE) was assessed by quantifying the amount of drug not encapsulated in the lipid nanoparticles. In brief, the TAC SLNs-ISG dispersion was centrifuged at 6000 rpm for 30 minutes at 4°C, and the TAC content in the supernatant was measured. The supernatant was dissolved in a 1:1 mixture of acetone and 0.1% acetic acid and analyzed by HPLC. Free drug concentration in the supernatant was determined spectrophotometrically at 210 nm. All measurements were performed in triplicate, and the entrapment efficiency was calculated using the following formula:

$$EE\%=W_{TAC}/(W_{SLNs\text{-}ISG}+W_{TAC})\times 100\% \quad (1)$$

Viscosity measurements

The sol–gel transition temperature of the TAC SLNs-ISG was evaluated using the tube inversion method [24]. Twenty milliliters of the formulation were placed in a vial and immersed in an oil bath at various temperatures until equilibrium was reached. The vial was inverted, and if the sample did not flow within 30 seconds, it was considered a gel. Temperature increments of 2°C were applied at each step. Viscosity of the formulation, both in sol and gel states, was measured with a rotating viscometer (60 rpm, rotor 2), using appropriate spindles depending on the viscosity range, with readings taken directly from the instrument display.

In vitro drug release

Drug release from TAC SLNs-ISG was studied using a dynamic dialysis method. Twenty milligrams of the formulation were placed in dialysis bags, which were then immersed in 2000 mL of simulated tear fluid (STF; 0.67 g NaCl, 0.20 g $NaHCO_3$, 0.008 g $CaCl_2 \cdot 2H_2O$ in 100 mL distilled water). The system was maintained at 37°C with agitation at 75 rpm in a thermostatic oscillator. Samples (1 mL) were withdrawn at predetermined time points (0.25, 0.5, 1, 2, 4, 6, 8, 12, and 16 h) and replaced with fresh medium. The amount of drug released was quantified by HPLC. Free TAC and TAC SLNs were used as controls for comparison.

Stability studies

The stability of TAC SLNs-ISG was evaluated according to ICH guidelines under conditions of 40°C and 75% relative humidity. Three batches of the formulation were assessed. Samples were collected at 0, 1, and 3 months, and 0.1 mL aliquots were analyzed for drug content by HPLC. Additional parameters related to stability were also monitored during this period.

In vivo pharmacokinetics

Ocular disposition of TAC SLNs-ISG, TAC SLNs, and TAC eye drops (0.1% w/v) was assessed in New Zealand rabbits (2–3 kg). Rabbits were acclimatized for one week prior to the experiment. A 50 µL dose of each formulation was instilled in the cul-de-sac of the right eye, while the left eye served as a control. Tear samples (≈5 µL) were collected at 15, 30 min, 1, 2, 4, 5, 6, 8, and 10 hours using a micropipette. After 10 hours, rabbits were euthanized with intravenous pentobarbital. Eyes were rinsed with cold DPBS, tissues were excised, and stored at −80°C until analysis. Tear samples were extracted in a 1:1 acetone:0.1% acetic acid mixture and analyzed via HPLC. Ocular tissues were processed by acetone precipitation and analyzed using LC-MS/MS on a Genesis C18 column with gradient elution. TAC was detected using Turbo Ionspray in positive mode (m/z 807.5 → 772.4), with good linearity over 10–10,000 ng/mL ($r^2 = 0.996$) and a lower quantitation limit of 0.1 ng/mL, indicating high sensitivity and reliability.

Pharmacodynamic evaluation

The therapeutic effect of TAC SLNs-ISG was investigated in BALB/c mice. Mice were divided into five groups: A – normal (no treatment), B – PBS control, C – 0.1% TAC eye drops, D – 0.1% TAC SLNs, and E – 0.1% TAC SLNs-ISG.

1. *Sensitization stage:* On day 1, mice received intraperitoneal injections of ovalbumin (OVA, 100 µg) with $Al(OH)_3$ (35 µg) in 200 µL PBS.
2. *Immune intervention stage:* From day 7, eyes of groups B–E were treated with their respective formulations three times daily for five days.
3. *Stimulation stage:* OVA solution (10 µL, 5 mg/mL) was administered to induce immune conjunctivitis. Clinical symptoms were scored daily for seven days using biomicroscopic examination, with three independent parameters each rated from 0 (none) to 3+ (severe), yielding a maximum score of 9+.

After OVA challenge, mice were treated once daily for five days with their respective formulations. Clinical scores were recorded, and ocular levels of OVA-specific IgE, IFN-γ, and IL-4 were measured to assess immunological response.

Table 1. Scoring of Conjunctivitis Signs and Symptoms

Symptom	Score 0 (None)	Score 1 (Mild)	Score 2 (Moderate)	Score 3 (Severe)
Conjunctival injection	None (−)	Pink conjunctiva	Distinct red conjunctiva	Intense dark red conjunctiva
Eyelid swelling (Blepharoptosis/edema)	None (−)	Swelling limited to lower eyelid	Swelling of both upper and lower eyelids with partial eyelid closure	Severe swelling with ectropion and near-complete or complete eyelid closure
Ocular discharge/secretion	None (−)	Small amount of mucoid secretion	Eyelashes around the lids are wet	Eyelashes and surrounding hairs are wet, matted, and sticky with discharge

Histological analysis of corneal tissue

Corneal samples from all experimental groups were collected and subjected to detailed histopathological examination to assess tissue integrity and morphological changes. All animal experiments were conducted in compliance with institutional ethical guidelines and approved by the Ethics Committee of Chongqing Medical University (Protocol No. 19A2040). The procedures strictly adhered to the National Institutes of Health (NIH) standards for laboratory animal care and use [1].

Evaluation of corneal drug permeability

The permeability of tacrolimus formulations was evaluated using isolated rabbit corneas. Whole eyes were transported in ice-cold Hanks' balanced salt solution overnight to maintain tissue viability. Upon arrival, the corneas were carefully dissected and rinsed in chilled Dulbecco's phosphate-buffered saline (DPBS, pH 7.4). Each cornea was mounted on a Valia-Chien diffusion cell with the epithelial surface facing the donor compartment. The experimental setup was maintained at 32°C with a circulating water bath to mimic ocular surface conditions [2].

For testing, 1 mL of TAC (0.1% w/v) in eye drops, SLNs, or SLNs-ISG was applied to the donor chamber. The receiver chamber contained 5 mL of DPBS with 5% hydroxypropyl beta-cyclodextrin (HPβCD) and was continuously stirred to ensure homogeneous distribution. Samples of 500 µL were collected from the receiver compartment at predetermined time points over a 2-hour period and replaced with an equal volume of fresh buffer to maintain sink conditions. All samples were stored at −80°C until quantification by high-performance liquid chromatography (HPLC). Experiments were performed in triplicate to ensure reproducibility and accuracy [3].

The cumulative amount of TAC was calculated as per the equation:

$$M_n = V_r C_{r(n)} + \sum_{x=1}^{x=n} V_{S(X-1)} C_{r(x-1)} \quad (2)$$

In this equation, **n** represents the specific sampling time point, Vr is the total volume of the receiver chamber (mL), Vs is the volume of the aliquot withdrawn at the nth time point (mL), and Cr(n) denotes the concentration of the drug in the receiver medium at that time (µg/mL).

The rate of TAC transported across rabbit cornea was calculated using the slope of the cumulative amount of TAC transported versus time plot. The steady state flux of TAC was determined using the following equation:

$$Flux(J) = (dM/dt)/A \quad (3)$$

Statistical analysis

Data were evaluated using extreme value analysis and ANOVA. SPSS software was employed for statistical computations, and differences were considered significant when $p < 0.05$.

Results and Discussion

Preparation and characterization

The primary aim of this study was to develop SLNs and the corresponding in situ gel to slow the clearance of TAC in the eye and enhance drug absorption. Based on the solubility of TAC in the lipid phase—using GMS and Compritol 888 ATO as lipid components—Tween 80 and glycerol were chosen for the aqueous phase to design, prepare, and optimize the SLN formulation [25].

TAC-SLNs-ISG were produced using homogenization followed by probe sonication. Key physicochemical properties, including particle size and encapsulation efficiency (EE%), are summarized in **Table 2**. The mean particle size of TAC-SLNs-ISG was 122.3 ± 4.3 nm. Compared to TAC-SLNs, the in situ gel formulation did not significantly alter particle size. It is generally accepted that a PDI value between 0.01 and 0.5 indicates a sufficiently narrow size distribution. The PDI of TAC-SLNs-ISG was 0.21, indicating a relatively uniform formulation with high throughput and favorable permeability, consistent with the in vitro release results [25].

Table 2. The Characteristics of TAC-SLNs ISG and TAC-SLNs

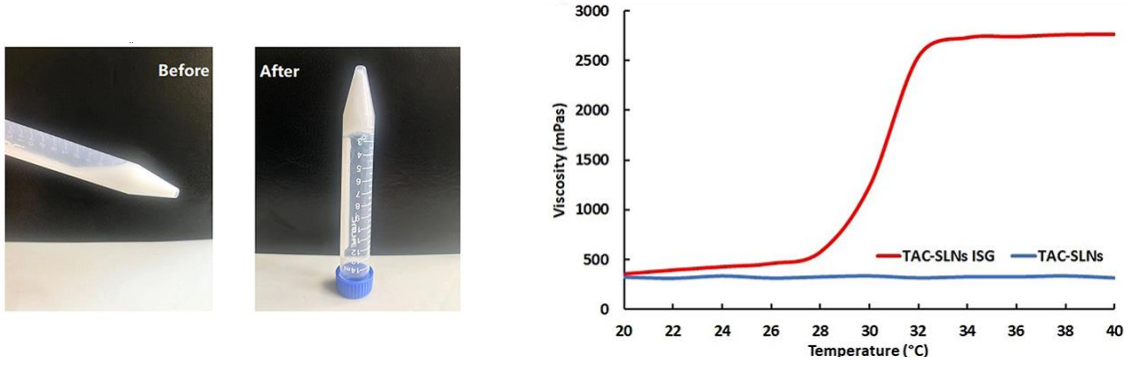
Parameters	TAC-SLNs	TAC-SLNs ISG		
		0 m	1 m	3 m
Particle size (nm)	121.5 ± 3.8	122.3 ± 4.3	125.5 ± 5.1	127.4 ± 5.4
Encapsulation efficiency (%)	84.6±6.2	85.9±7.2	84.4±6.7	82.6±4.3
Polydispersity index	0.24	0.21	0.24	0.26
Zeta potentials (mV)	−23.7±3.8	−26.8±3.4	−28.4±4.1	−29.3±4.5

Note: (n=3).

Viscosity experiments

The viscosity of ophthalmic formulations plays a crucial role in extending their precorneal residence time, which is essential for improving ocular drug absorption. Considering ocular physiology, the shear rate encountered during eyelid and eyeball movements varies widely, from 0.03–0.14 s^{-1} during inter-blink periods to 4,250–28,500 s^{-1} during a blink. Therefore, the formulation's viscosity should not interfere with the pseudoplastic nature of the tear film [26]. Polymers exhibiting pseudoplastic behavior are recommended for ocular gels [27], and multiple studies have shown that poloxamer-based gels demonstrate pseudoplastic characteristics [28, 29].

To investigate the effect of temperature on gelation, the viscosity of TAC-SLNs-ISG was measured. The results indicated that TAC-SLNs-ISG behaves as a typical pseudoplastic system, with viscosity increasing significantly as temperature rises, ultimately forming a rigid gel. The gelation temperature of this thermoresponsive formulation was determined to be 32°C **(Figure 1)**. In contrast, the viscosity of the TAC-SLNs suspension remained relatively low and stable with temperature changes.



a) b)

Figure 1. (a) Photographs of in situ gels formed before (4°C) and after (37°C) gelation. (b) Mean viscosity-temperature trends profiles of TAC SLNs and TAC SLNs-ISG. (n=3).

In vitro release

The drug release profiles of TAC-SLNs-ISG, TAC-SLNs, and free TAC are presented in **Figure 2**. By the end of the experiment, approximately 80% of the drug was released from the TAC-SLNs, whereas only 56% was released from the TAC-SLNs-ISG formulation. The release pattern of TAC-SLNs-ISG followed a biphasic model: an

initial rapid release phase, with nearly 30% of TAC released within the first hour, followed by a slower, sustained release phase. This early burst release is primarily due to the drug present on or near the gel surface, while the later sustained release is attributed to the gradual diffusion and dissolution of the drug from the lipid matrix and polymer network. As summarized in **Table 3**, the Higuchi model ($Q = 9.287\ t^{1/2} – 2.263$, $r = 0.994$) best described the release kinetics of TAC-SLNs-ISG. These results suggest that the sustained-release behavior of TAC-SLNs-ISG could potentially improve ocular drug absorption [25].

Table 3. Release Kinetic of TAC SLNs-ISG

	TAC SLNs-ISG	
	Equation	**Correlation Coefficient (R)**
Zero-order	Q =4.312t+0.217	0.931
First-order	Ln(1–Q) =−3.287t+0.673	0.971
Weibull	lnln(1/(1–Q)) =4.938 lnt+1.332	0.954
Higuchi	Q =9.287t1/2-2.263	0.994

Note: (n=6).

Stability studies

Over a storage period of three months, the formulations exhibited minimal changes in viscosity. HPLC analysis of the samples (data not shown) demonstrated that drug degradation was negligible, with less than 5% of TAC decomposed. Additional stability parameters are summarized in **Table 2** [25].

In vivo kinetics

The tear fluid concentration–time profiles following ophthalmic administration of the different formulations in rabbits are illustrated in **Figure 3**, with corresponding AUC parameters presented in **Table 4**. For TAC eye drops, the peak concentration (C_max) of 4657.7 ng/mL was reached at 30 minutes (T_max). In contrast, the TAC-SLNs formulation reached a maximum concentration of 1892.6 ng/mL at 30 minutes, whereas TAC-SLNs-ISG achieved its peak (2132.3 ng/mL) after 2 hours, indicating a delayed Tmax for the in situ gel. Although the C_max values for TAC-SLNs and TAC-SLNs-ISG were significantly lower ($p < 0.05$) than those for conventional eye drops, the AUC_{0}–t for TAC-SLNs-ISG was 590,355.9 ng•min/mL—approximately 2.65 times higher than the AUC_{0}–t of 222,382.5 ng•min/mL observed with TAC eye drops—highlighting the improved ocular bioavailability offered by the in situ gel system. The enhanced performance is likely due to active uptake of SLNs by corneal and conjunctival cells, in addition to passive drug diffusion. Enzymes such as lipases present in the tear film and epithelial cells contribute to the controlled release of TAC from the lipid matrix, allowing drug release both on the ocular surface and within the corneal tissue. These findings underscore the sustained-release characteristics of TAC-SLNs-ISG in vivo [25].

Table 4. Ocular Tear Pharmacokinetic Parameters of TAC in Tear versus Time Profiles in 600 Min for Various Formulations

Formulation	**Cmax (ng/mL)**	**Tmax (h)**	**MRT (h)**	**T1/2 (h)**	**AUC0–t (ng·min/mL)**	**AUC 0-t Ratio**
TAC eye drops	4657.7±412.2	30.2±4.3	1.28±0.45	1.84±0.76	222,382.5 ± 20,192.5	–
TAC-SLNs	1892.6±206.4*	33.6±8.9	2.07±0.92	3.72±0.88*	339,555.4 ± 31,927.2*	1.53
TAC-SLNs-ISG	2132.3±241.6*	120.6±11.6*	2.82±1.21*	3.92±0.94*	590,355.9 ± 57,281.7*	2.61

Notes: Each value represents the mean ± SD of three determinations. *p<0.05 (compared to TAC eye drops). (n=6).

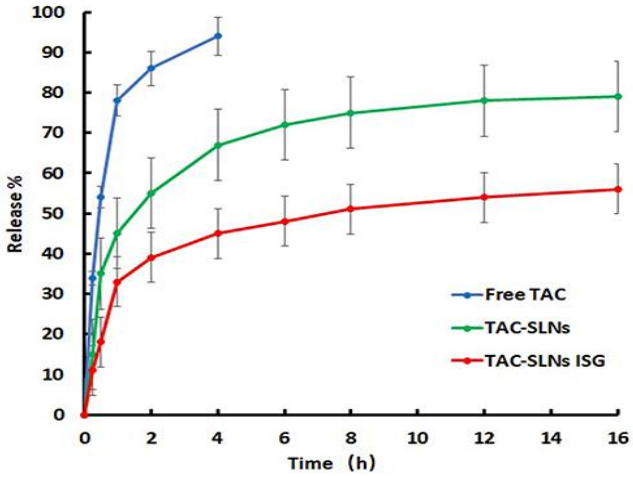


Figure 2. The in vitro drug release profiles of TAC eye drops, TAC SLNs and TAC SLNs-ISG. Number represents the percentage of release. (n=6).

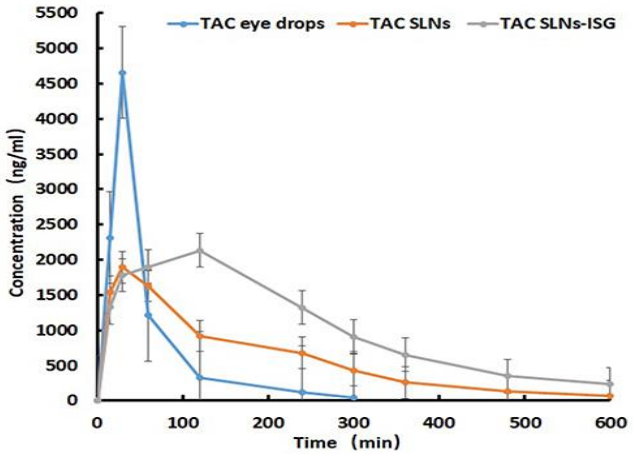


Figure 3. Concentration-time curve of TAC in different formulations (TAC eye drops, TAC SLNs and TAC SLNs-ISG). (n=6).

Pharmacodynamic evaluation

The establishment of the animal model in this study was completely successful, and there were significant differences between the positive control group and the negative control group **(Figure 4)**.

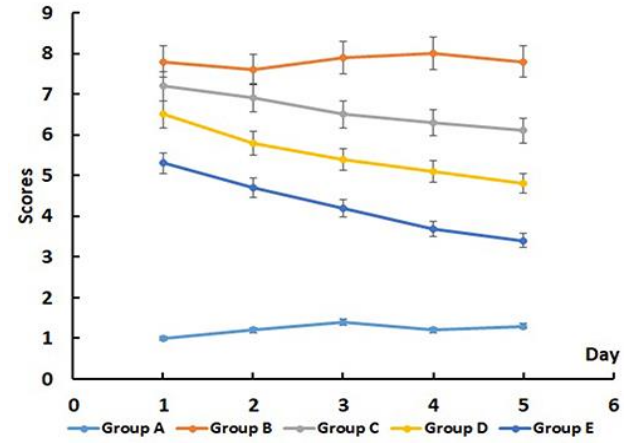


Figure 4. The pharmacodynamic scores in different groups. Group A: Normal (untreated, positive control); Group B: PBS (negative control); Group C: 0.1% TAC eye drop; Group D: 0.1% TAC-SLNs; Group E: 0.1% TAC-SLNs ISG. (n=6).

In the untreated group (Group A), symptoms were minimal, and the corresponding scores remained consistently low throughout the observation period. In contrast, the positive control group (Group B) displayed pronounced symptoms, with scores consistently high. In this study, all groups received their treatments in the morning, and symptom scoring was conducted in the afternoon, which led to significant differences between the experimental groups on the first day post-treatment. Over time, all three treatment groups (Groups C, D, and E) exhibited varying degrees of symptom reduction, with Group E showing the most substantial improvement. By day five, the alleviation of symptoms in Group E was particularly pronounced. The relatively short ocular retention of conventional eye drops and TAC-SLNs likely contributed to the more modest effects observed in those groups.

Biochemical analyses of OVA-specific IgE, IFN-γ, and IL-4 levels revealed that Group E demonstrated significantly better therapeutic outcomes for immune conjunctivitis compared to the other control groups ($p < 0.05$), **(Figure 5)** [25]. TAC exerts its effects by inhibiting activation and degranulation of conjunctival mast cells, thereby suppressing the release of inflammatory mediators. It also downregulates serum IL-4, reducing the B cell-mediated switch from IgM to IgE and decreasing IgE synthesis. Additionally, by upregulating IFN-γ levels, TAC inhibits Th2 cell proliferation and IL-4 activity, limiting Th1-to-Th2 conversion and maintaining a dynamic Th1/Th2 balance. This mechanism effectively controls type I allergic responses, offering therapeutic benefits for immune conjunctivitis. Optimization of the drug delivery system, such as using SLNs or in situ gels, further enhances the therapeutic efficacy. Histopathological analysis of corn

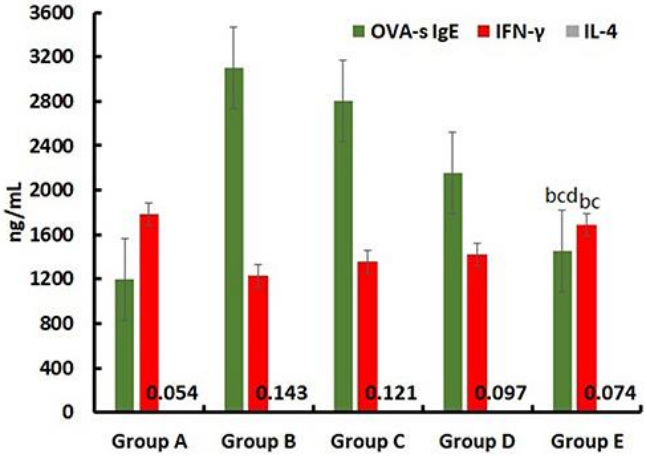
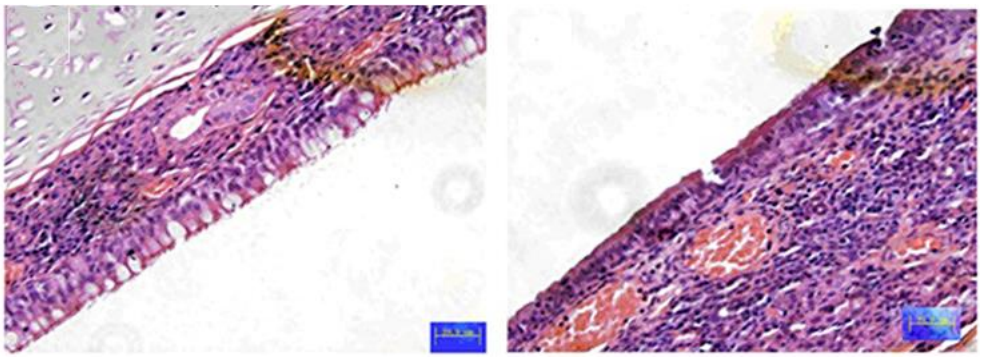
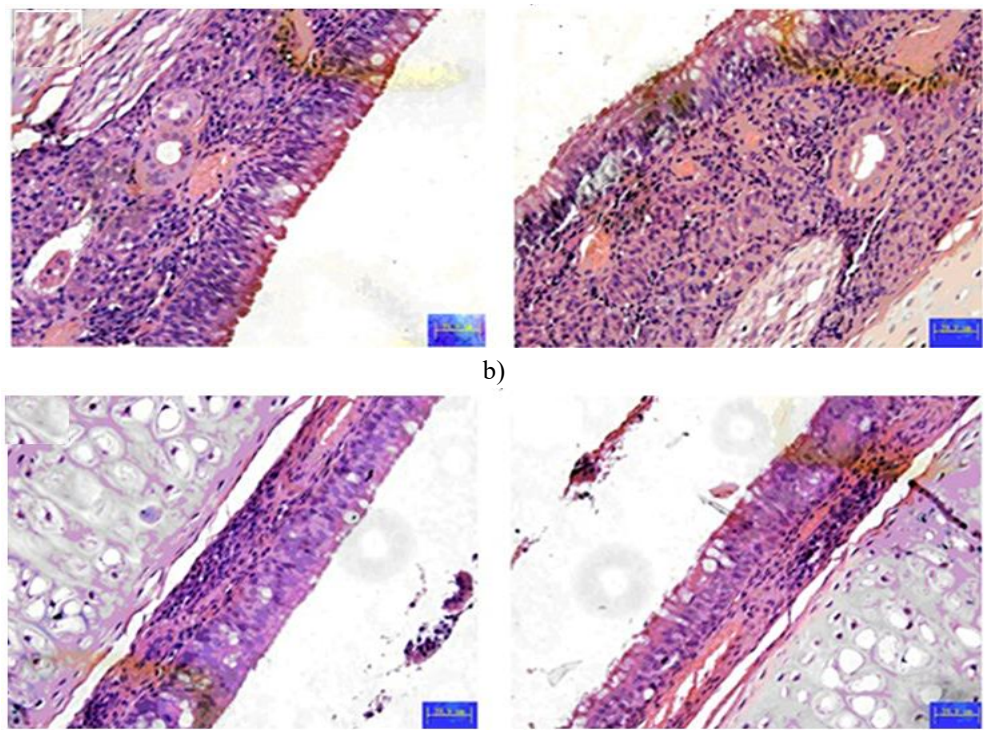


Figure 5. OVA-s IgE, IFN-γ and IL-4 concentration of different treatment groups in mice after pharmacodynamic study. Group A: Normal (untreated, positive control); Group B: PBS (negative control); Group C: 0.1% TAC eye drop; Group D: 0.1% TAC-SLNs; Group E: 0.1% TAC-SLNs ISG. (n=6). $^{b}p<0.05$, Group E vs Group B; $^{c}p<0.05$, Group E vs Group C; $^{d}p<0.05$, Group E vs Group B



a)



b)

c)

Figure 6. Histopathological studies of corneal tissue of different groups. (a) normal; (b) TAC SLNs (c) TAC SLNs-ISG. Left: treatment eye; Right: un-treatment eye.

Permeability test

The transcorneal permeability and flux values of TAC in the different formulations—eye drops, SLNs, and SLNs-ISG—are summarized in **Table 5**. The results indicate that TAC delivered via SLNs exhibited significantly higher permeability and flux across intact corneal tissues compared to conventional eye drops. This suggests that lipid-based nanoparticles can effectively enhance drug penetration through the cornea. In contrast, TAC in the SLNs-ISG formulation showed slightly reduced flux and permeability relative to SLNs, which can be attributed to the controlled and sustained release properties conferred by the higher viscosity of the in situ gel [25].

Table 5. Permeability and flux of different TAC formulations.

Formulation	Permeability (*10^{-6} cm/sec)	Flux (µg/min/cm^2)
TAC eye drops	0.91±0.08	0.062±0.007
TAC-SLNs	9.15±1.34*	0.12±0.04*
TAC-SLNs-ISG	8.26±0.73*	0.065±0.004

Notes: Each value represents the mean ± SD of three determinations. *p<0.05 (compared to TAC eye drops). (n=6).

Conclusion

This study focused on the development of a novel in situ gel formulation of tacrolimus-loaded solid lipid nanoparticles (TAC-SLNs-ISG) for ocular drug delivery. The TAC-SLNs-ISG were successfully prepared using a combination of homogenization and probe sonication techniques. The formulation exhibited an average particle size of 122.3 ± 4.3 nm, and incorporation into the in situ gel did not significantly alter particle size compared to TAC-SLNs [25]. Viscosity measurements indicated that the gel displayed typical pseudoplastic behavior, with a notable increase in viscosity as temperature rose, eventually forming a rigid gel at 32°C [26–29]. Both in vitro and in vivo evaluations demonstrated sustained drug release from TAC-SLNs-ISG, while animal studies confirmed enhanced pharmacodynamic performance relative to conventional eye drops and TAC-SLNs. Overall, these findings suggest that TAC-SLNs-ISG holds considerable promise as an effective ocular drug delivery system [25]

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Conflict of Interest: None

Financial Support: None

Ethics Statement: None

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