



## METHODS OF USING PILOCARPINE AND POLYMERS IN OCULAR DRUG DELIVERY SYSTEM: A REVIEW

**B. Premkumar\*, M. D. Swetha, S. Mohamed Shehal, G. Saroj, P. R. Roshan Khumaar, D. Keshika, M. Pradeepkumar, K. Samunesh and K. Karthick**

Department of Pharmaceutics & Biotechnology, Sree Abirami College of Pharmacy, Eachanari, Coimbatore - 641 021, Tamil Nadu, India. [Affiliated to The Tamil Nadu Dr. M. G. R. Medical University, Chennai].



\*Corresponding Author: Dr. B. Premkumar

Department of Pharmaceutics and Biotechnology, Sree Abirami College of Pharmacy, Eachanari, Coimbatore - 641 021, Tamil Nadu, India. [Affiliated to The Tamil Nadu Dr. M. G. R. Medical University, Chennai].

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### ABSTRACT

Ocular drug delivery poses significant challenges due to physiological barriers such as tear fluid turnover, blinking, and limited corneal permeability, which hinder effective drug absorption. Pilocarpine, a cholinergic agent widely used for the management of glaucoma and other ocular conditions, demonstrates poor bioavailability when administered through conventional eye drops, necessitating frequent dosing and causing potential side effects. To overcome these limitations, polymer-based drug delivery systems have emerged as promising alternatives, offering controlled and sustained release of drugs while enhancing ocular retention and bioavailability. This review explores various methods of incorporating pilocarpine into polymeric carriers for ocular delivery, including nanoparticles, microspheres, hydrogels, and mucoadhesive systems. Each method presents unique advantages: nanoparticles enhance corneal penetration, hydrogels offer prolonged retention, and mucoadhesive polymers improve contact time with ocular tissues. The integration of pilocarpine with advanced polymeric technologies holds great potential to improve therapeutic outcomes in glaucoma treatment and reduce dosing frequency, making ocular therapy more effective and patient-friendly.

**KEYWORDS:** Ocular drug delivery, polymeric carriers, nanoparticles, microspheres, hydrogels.

### INTRODUCTION

Effective ocular drug delivery remains a major challenge in pharmaceutical sciences due to the eye's complex protective mechanisms.<sup>[1,2]</sup> The presence of dynamic barriers such as blinking, tear drainage, and limited corneal permeability significantly reduces the residence time and absorption of topically applied drugs.<sup>[2]</sup>

Pilocarpine, a parasympathomimetic agent commonly used for the treatment of glaucoma and ocular hypertension, is traditionally administered in the form of eye drops.<sup>[3]</sup> However, its therapeutic efficiency is limited by poor bioavailability, rapid precorneal drug loss, and the need for frequent administration, which can reduce patient compliance and increase the risk of side effects.<sup>[4]</sup>

To address these challenges, novel polymer-based drug delivery systems have been developed to improve the ocular retention and sustained release of pilocarpine.<sup>[5]</sup> Polymers offer versatile platforms for controlled drug delivery, enhancing drug stability, prolonging residence time, and minimizing systemic absorption.<sup>[6]</sup> Various formulations, including nanoparticles, microspheres,

hydrogels, and mucoadhesive systems, have been investigated for their potential to improve pilocarpine delivery.

#### Advantages

##### 1. Improved Bioavailability

- Polymers enhance the residence time of pilocarpine on the ocular surface, leading to better drug absorption.<sup>[6]</sup>

##### 2. Sustained and Controlled Release

- Allows for gradual drug release, reducing the need for frequent dosing.<sup>[7]</sup>

##### 3. Reduced Side Effects

- Controlled delivery minimises systemic absorption and local irritation.<sup>[8]</sup>

##### 4. Enhanced Patient Compliance

- Less frequent administration leads to greater convenience and adherence to treatment.

##### 5. Targeted Drug Delivery

- Some polymer systems (e.g., nanoparticles) can

penetrate ocular tissues more effectively, delivering pilocarpine directly to the target site.<sup>[9]</sup>

## 6. Protection of Drug Molecules

- Polymers can shield pilocarpine from degradation caused by enzymes or environmental factors.<sup>[10]</sup>

## 7. Versatile Formulation Options

- Various forms like hydrogels, nanoparticles, or mucoadhesive inserts can be customised to suit specific clinical needs.

## DISADVANTAGES

### 1. Complex Formulation Process

- Requires advanced techniques and equipment for preparation and optimization.

### 2. Potential Ocular Irritation

- Some polymers or additives may cause discomfort or allergic reactions.

### 3. Stability Issues

- Certain polymer-drug combinations may face stability problems during storage.

### 4. Cost-Intensive Development

- Research, development, and production of polymer-based systems can be expensive.

### 5. Regulatory Hurdles

- Novel delivery systems may face longer approval times due to the need for extensive safety and efficacy data.

### 6. Scalability Challenges

- Difficulties in translating lab-scale formulations to mass production.

## Methodology (Formulation Methods)

Polymer-based ocular drug delivery methods enhance the bioavailability and efficacy of pilocarpine by overcoming ocular barriers and providing sustained release. Below are the major formulation strategies explained in detail:

### 1. Nanoparticles Formation (e.g., PLGA, Chitosan) Techniques

- **Solvent Evaporation:** Pilocarpine and polymer (e.g., PLGA) are dissolved in a volatile organic solvent. This solution is emulsified in an aqueous phase containing a surfactant. The solvent is then evaporated, leading to the formation of solid nanoparticles.
- **Nanoprecipitation:** A polymer-drug solution in a solvent is dropped into a non-solvent under stirring. Nanoparticles spontaneously form due to rapid diffusion and precipitation.
- **Ionic Gelation:** Common with natural polymers like chitosan. Positively charged chitosan interacts with negatively charged crosslinkers (e.g.,

tripolyphosphate) to form nanoparticles at room temperature.

## Benefits

- Enhanced corneal penetration due to small size (<200 nm)
- Sustained release of pilocarpine
- Protection from enzymatic degradation
- Can be surface-modified for targeted delivery

## 2. Microsphere Encapsulation

### Techniques

- **Emulsion-Solvent Evaporation:** Pilocarpine and polymer are dissolved/dispersed in an organic solvent and emulsified into an aqueous phase. Upon solvent removal, microspheres are formed.
- **Spray-Drying:** A solution or suspension of drug and polymer is atomized into a hot drying chamber, forming solid microspheres as the solvent rapidly evaporates.

### Benefits

- High drug loading capacity
- Prolonged drug release (days to weeks)
- Ideal for reducing administration frequency

### Challenges

- Requires careful optimization of size and drying parameters
- Not suitable for thermolabile drugs in spray-drying

## 3. Hydrogel Preparation

### Techniques

- **In Situ Gelation:** Liquid formulations undergo sol-to-gel transformation upon contact with ocular environment (pH change, temperature, or ionic concentration).
- **Thermo-sensitive Polymers:** Poloxamers gel at ocular surface temperature (~35 °C).
- **pH-sensitive Polymers:** Gellan gum or carbopol gel in response to tear pH (~7.4).

### Benefits

- Comfortable for the patient due to ease of application as drops
- Gel prolongs drug retention on ocular surface
- Provides sustained release for several hours

## 4. Mucoadhesive Systems

### Polymers Used

- **Carbopol, Hydroxypropyl Methylcellulose (HPMC), Sodium Alginate Mechanism**

These polymers form weak hydrogen bonds or electrostatic interactions with mucin on the ocular surface, enhancing residence time.

### Benefits

- Improved bioavailability due to extended contact with eye surface
- Better retention in patients with dry eyes or

- increased tear turnover
- Can be formulated as gels, inserts, or films

### Challenges

- Risk of irritation depending on polymer concentration and molecular weight

## 5. Ocular Inserts/Films

### Methods

- **Solvent Casting:** A polymer-drug solution is poured into a mold and dried, forming thin films.
- **Compression Molding:** Polymers are compressed with heat and pressure to shape inserts.

### Benefits

- Precise control over drug dose
- Long duration of action (days to weeks)
- Excellent for chronic conditions like glaucoma

### Challenges

- Insertion discomfort
- Patient acceptability varies

### Evaluation Parameters

To assess the efficiency, safety, and therapeutic viability of pilocarpine-loaded polymer systems, the following parameters are evaluated:

#### 1. Drug Loading and Encapsulation Efficiency

##### Definition

- **Drug Loading (%):** Amount of pilocarpine in formulation relative to the total weight.
- **Encapsulation Efficiency (%):** Percentage of pilocarpine successfully entrapped in the delivery system during formulation.

##### Method

UV-Vis or HPLC analysis of drug content post extraction.

##### Importance

Determines dose accuracy and economic feasibility.

#### 2. Particle Size and Surface Morphology

##### Tools Used

- **Dynamic Light Scattering (DLS):** Measures size distribution and zeta potential.
- **Scanning Electron Microscopy (SEM)/Transmission Electron Microscopy (TEM)**

Visualizes shape, surface, and porosity.

##### Importance

- Size affects ocular penetration and release rate
- Smooth, spherical particles enhance stability and ease of administration

#### 3. In Vitro Drug Release Studies

##### Method

- **Dialysis membrane method or Franz diffusion cells** simulate drug release into tear fluid.
- Samples are withdrawn at regular intervals and

analyzed via UV or HPLC.

##### Importance

Evaluates release kinetics (zero-order, first-order, Higuchi, Korsmeyer-Peppas models) and predict in vivo performance.

#### 4. Sterility Testing

##### Purpose

Ensures absence of microbial contamination, which is critical for ocular applications.

##### Method

- Membrane filtration or direct inoculation method as per pharmacopeial guidelines (USP, IP).
- Incubation in thioglycolate and soybean-casein digest media.

#### 5. pH, Viscosity, and Osmolarity Measurement

##### Instruments

- **pH Meter, Viscometer, Osmometer Importance:**
- Must match physiological tear fluid (pH ~7.4, osmolarity ~300 mOsm/kg)
- Viscosity affects spreadability and retention
- Ensures patient comfort and compatibility

#### 6. Bioadhesion and Swelling Studies

##### Method

- Evaluates the time a hydrogel or mucoadhesive system adheres to mucosal tissue
- Swelling studies assess gel expansion over time in simulated tear fluid

##### Importance

- Directly correlates with residence time and drug retention
- Ensures formulation stability

#### 7. In Vivo Ocular Irritation Test (Draize Test)

##### Model

- Rabbit eye model is commonly used.

##### Assessment

- Observations for redness, swelling, discharge, and corneal damage after instillation.

##### Importance

- Ensures formulation is non-irritating and safe for long-term use.

**Ethical Note:** Should comply with ethical standards and 3Rs (Replace, Reduce, Refine)

#### 8. Pharmacokinetic and Therapeutic Efficacy Evaluation

##### In Vivo Studies

- Evaluate pilocarpine concentration in aqueous humor or plasma over time
- Measure pharmacodynamic markers like Intraocular Pressure (IOP) reduction **Model:**

- Rabbits or other validated animal models

#### Importance

- Confirms systemic absorption, bioavailability, and therapeutic outcomes
- Supports clinical translation

#### Applications

##### 1. Treatment of Glaucoma

- Sustained pilocarpine release to reduce intraocular pressure (IOP).

##### 2. Management of Ocular Hypertension

- **Controlled delivery helps maintain consistent drug levels.**

##### 3. Post-Surgical Eye Care

- **Hydrogels or inserts for anti-inflammatory action and healing support.**

##### 4. Dry Eye and Other Chronic Eye Conditions

- Mucoadhesive systems prolong drug action in dry or compromised tear film.

##### 5. Potential for Combination Therapies

- Polymers can co-deliver pilocarpine with other drugs (e.g., beta-blockers).

#### CONCLUSION

The integration of polymer-based drug delivery systems has opened new avenues in enhancing the ocular delivery of pilocarpine, a widely used therapeutic agent for glaucoma and related conditions. Traditional eye drops formulations suffer from poor bioavailability, rapid drug clearance, and the need for frequent dosing, which can reduce treatment effectiveness and patient compliance. By incorporating pilocarpine into advanced polymeric carriers such as nanoparticles, hydrogels, microspheres, and mucoadhesive systems, researchers have demonstrated significant improvements in sustained release, ocular retention, and targeted drug delivery. These systems not only improve therapeutic outcomes but also minimize side effects and enhance patient comfort. Despite certain formulation and regulatory challenges, polymeric approaches present a promising future for ocular drug delivery. Continued research and development in this field will likely lead to more effective, patient-friendly, and commercially viable treatments, making a significant impact on the management of chronic eye diseases such as glaucoma.

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