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Original Article

Co-Delivery of Luminescent C-dots and Clonidine Hydrochloride Loaded Nanocarriers for the Effective Management of Glaucoma

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ABSTRACT

Aim/Background: Glaucoma is an eye illness associated with Intraocular Pressure (IOP) that, if untreated, can lead to significant vision impairments and potentially complete blindness. Research indicates that eye infections can elevate Intraocular Pressure (IOP) and lead to glaucoma, with anti-glaucoma treatments being ineffective. Combination therapy, which entails the administration of pharmaceuticals alongside nanoscale antibacterial agents, may serve as an effective alternative in this context. This work created a polymeric Nanocarrier (NCs) for the simultaneous topical delivery of fluorescent Carbon dots (C-dots) and Clonidine Hydrochloride (CH) for the treatment of infection and glaucoma. **Materials and Methods:** A polymeric nanocarrier was developed using the solvent evaporation method to simultaneously transport fluorescent Carbon Dots (C-dots) and Clonidine Hydrochloride (CH). C-dots were detected using UV-vis and fluorescence spectroscopy. Scanning Electron Microscopy (SEM) was employed to ascertain the dimensions and morphology of NCs. Additionally, Gram-negative *E. coli* bacteria were utilized in antibacterial studies. *Ex vivo* permeation and corneal hydration assessments were conducted on goat eyes, whereas *in vivo* investigations were performed on rabbit eyes. Fluorescence tests demonstrated that when activation by UV radiation, C-dots emitted blue light at a wavelength of 450 nm. **Results:** This was done after the synthesized C-dots were placed into 125 nm polymeric nanocarriers along with the medication. According to release studies, in physiological conditions, up to 95% of medicines are released in 60 min. **Conclusion:** In a study on corneal hydration, the nanocarriers exhibited effective hydration, which is essential for their bioavailability. The C-dots exhibited significant antibacterial efficacy against *E. coli* bacteria. The Intra Ocular Pressure (IOP) of the eye markedly diminished in *in vivo* testing relative to blank and commercial formulations for duration of up to 4 hr. The findings indicated that C-dots and clonidine hydrochlorides are suitable for treating glaucoma and secondary bacterial infections when administered concurrently through nanocarriers.

Keywords: Glaucoma, C-dots, Clonidine Hydrochloride, Nanocarrier, Intraocular Pressure.

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INTRODUCTION

Glaucoma is a chronic disorder that impacts the anterior segment of the eye. The condition is defined by elevated Intraocular Pressure (IOP), resulting from heightened aqueous fluid production within the eye. This occurs due to excessive fluid production or insufficient fluid drainage from the eye.[1] The ganglionic retinal cells receive limited blood supply due to the eye's markedly elevated intraocular pressure, resulting in cellular degeneration, chronic optic nerve injury and ultimately irreversible vision loss. This is the primary cause of blindness and severe ocular disease that impacts millions of individuals globally.

Management of this illness necessitates lifelong anti-glaucoma medication.[2] To mitigate issues associated with Intraocular Pressure (IOP), clonidine, an α-2 adrenergic agonist, is commonly prescribed.[3] It diminishes aqueous humor production and enhances uveo-scleral outflow by stimulating prostaglandin synthesis. Numerous studies, primarily involving animals, indicate that clonidine possesses neuroprotective properties, a finding recently corroborated by research. A vital defense against photoreceptor degradation and oxygen-induced optic nerve injury seems to be the neuroprotective effect.

Moreover, when administered alongside -blockers, clonidine is recognized for its efficacy without adverse effects on cardiac or pulmonary function. Recent research has shown that certain

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clinically significant ocular infections, including Chlamydia trachomatis, can produce a substantial inflammatory response,[4] which similarly elevates Intraocular Pressure (IOP). Addressing the dysregulated pressure resulting from ocular infections is crucial alongside normal glaucoma management. Combination therapy, which entails the administration of pharmaceuticals alongside nanoscale antibacterial agents, may serve as an effective alternative in this context. Carbon Dots (C-dots) are nanoscale materials that can be utilized in conjunction with pharmaceutical compounds for the treatment of glaucoma and ocular infections. A new category of luminous nanomaterials, characterized by diameters under 10 nm, include carbon-based nanoscale materials, including Graphene Quantum Dots (GQDs) and Carbon Dots (C-dots). Carbon Dots (C-dots) have garnered heightened interest owing to their notable advantages, such as reduced toxicity, chemical inertness, adjustable fluorescence and favorable water solubility.[5,6]

Furthermore, C-dots were reported to exhibit significant bactericidal activity against both Gram-positive and Gram-negative microbes. An improved ocular drug delivery system is essential for the effective management of glaucoma, as the administration of medications into the eye presents significant challenges due to the eye's diminutive size and the limited volume dispersion of eye drops (5%). Eye drops represent the most effective drug delivery system for ocular treatment; yet, they are rapidly eliminated due to blinking, induced lacrimation, normal tear turnover and rapid pre-corneal clearance. The cornea, functioning as a barrier, along with these pre-corneal barriers, inflicted considerable damage to the injected ocular drugs. The aforementioned reasons render the enhancement of the ocular distribution of intravitreal medicines more compelling. A variety of conventional and innovative techniques have been established to overcome ocular obstacles and enhance ocular penetration.[7] The scientific community is closely monitoring polymeric nanocarrier-mediated ocular delivery systems because to their superior penetration, prolonged drug retention and improved bioavailability of pharmaceuticals. We have developed a polymeric nanocarrier for the concurrent delivery of fluorescent carbon dots (C-dots) and CH. The results indicated that Clonidine Hydrochloride (CH) and C-dots may serve as an effective treatment for glaucoma by reducing Intraocular Pressure (IOP) and bacterial infection.[8]

MATERIALS AND METHODS

Materials

The CH was obtained from FDC Ltd., in Mumbai, India. The Eudragit RL100 polymer was acquired from Indian Fine Chemicals, located near Mumbai. The methanol used in this study was procured from Merck Life Science Pvt. Ltd., located in Mumbai, India. Tween-80 was procured from SD Fine Chemical Ltd., Mumbai. The procurement of ethanol was facilitated by Merck Life Science Pvt. Ltd., a company based in Mumbai, Maharashtra. The Paracetamol and Polyethylene Glycol (PEG) used in this study were obtained from SRL chemicals, Mumbai. The acetone used in this study was obtained from Thermo Fisher Scientific Ltd.

Methods

Stock Solution Preparation

A stock solution of clonidine hydrochloride was prepared by dissolving 100 mg of the drug in 100 mL of methanol, yielding a concentration of 1000 µg/mL. The solution was diluted with the identical solvent to achieve a working concentration of 100 µg/mL, which was then employed for various research studies. To create the calibration curve, a drug solution at a concentration of 100 µg/mL was further diluted to achieve concentrations between 5 and 25 µg/mL. The absorbance of each dilution was then measured.

Preparation of luminescent C-dots

The synthesis of Carbon dots (C-dots) was conducted by employing paracetamol and Polyethylene Glycol (PEG) as precursor materials. These precursors were combined in a ratio of 3:1 and subjected to pulse heating for 30 sec using a microwave with a power output of 800 W. The heating process was carried out for a total duration of 2 min. A solution of the dark brown substance was acquired, which was subsequently diluted in distilled water and filtered using a Whatman Filter paper. In order to obtain C-dots with high purity and luminescence, the solution was subjected to further dialysis in distilled water for duration of 24 hr.

Preparation of drug-polymer suspension

Prior to the fabrication of polymer nanocarriers, a suspension of the polymer and drug was prepared to augment their interaction, hence enhancing the probability of successful encapsulation. A drug-polymer solution was prepared by blending 30 mg of Eudragit RL 100 polymer with 5 mg of clonidine hydrochloride in a solvent of methanol and acetone at a 1:3 ratio. Thereafter, the mixture was subjected to sonication and mild heating to obtain a uniform solution. The pH of the aforementioned organic phase was adjusted to about 4.0 by the addition of 0.1 N Hydrochloric acids (HCl). Simultaneously, 0.5 mL of Tween-80 was mixed with 19.5 mL of filtered water. The organic phase generated was subsequently amalgamated with the aqueous phase containing Tween-80, with the latter being added dropwise while stirring the mixture using a magnetic stirrer. The final volume was adjusted to 40 mL.

Preparation of C-dots and Drug loaded NCs

The synthesized drug-polymer combination was amalgamated with luminous C-dots (240 µL of a 10 mg/mL solution) and an equivalent volume of chloroform, leading to the establishment of an aqueous-organic bilayer. The mixture was subjected to

sonication at 30 sec intervals to prepare loaded nanocarriers. To attain the optimal synthesis of loaded nanocarriers[9,10] the solution underwent a freeze-thaw cycle, maintained at -20°C for 14 hr. Thereafter, the solution was allowed to reach room temperature to promote the evaporation of any remaining organic solvent. The nanocarriers were centrifuged at 8000 revolutions per minute for 5 min to collect and isolate them. The isolated nanocarriers were subsequently resuspended in Phosphate Buffer Saline (PBS) for additional biological research analysis.[11,12]

Characterization of Carbon Dots

Calibration Curve of Drug Clonidine Hydrochloride

To establish the calibration curve necessary for quantifying the drug concentration in an unknown sample, a series of drug solutions with increasing concentrations were generated. The absorbance values at the maximum wavelength (λ_{max}) of 210 nm were then measured using UV-vis spectroscopy.[13] A calibration curve was produced using the free drug concentration and its associated absorbance value.

Characterization of luminescent C-dots

The C-dots underwent investigation utilizing both a UV-visible spectrophotometer and a fluorescence spectrophotometer. The UV-visible spectrophotometer utilized in the investigation was a double beam Spectrophotometer-2202, produced by Systronic in India. The study's results revealed a peak at around 242 nm. The carbon dots (C-dots) displayed a pronounced blue emission upon exposure to Ultraviolet (UV) light, particularly when positioned beneath a transilluminator.[14] The fluorescence spectroscopy analysis utilized the Analytical FS 2060 equipment, demonstrating that the C-dots displayed a maximum emission wavelength (λ_{max}) of 450 nm when excited by UV light at 320 nm.

Antibacterial test of C-dots

The antibacterial efficiency of Carbon dots (C-dots) was examined utilizing *Escherichia coli*, a prototypical model for Gram-negative bacteria. The bacterial cultures were cultured in LB media at 37°C, with agitation from a shaking incubator working at 220 rpm. Prior to performing the bacterial test, all equipment was sterilized via an autoclave. In the antibacterial experiment, various concentrations (Dose-1: 50 µg/mL, Dose-2: 100 µg/mL and Dose-3: 200 µg/mL) of C-dots were administered to a 1% bacterial inoculum and incubated under standard growth conditions overnight. Bacterial growth was measured at the 12 hr interval by assessing the absorbance of the microplate reader at a wavelength of 595 nm. The experiments were performed in triplicate.[15,16]

Physicochemical Characterization

Determination of entrapment efficiency of drug and C-dots

The investigation of the loading of the C-dots and medicament was conducted through the use of UV-vis spectroscopy. During the manufacture of NC,[17,18] it was mentioned that a concentration of 10 mg/mL of C-dots was incorporated with 5 mg/mL of the medication. The nanocarriers[19] were precipitated using centrifugation at a speed of 8000 revolutions per minute for 5 min, resulting in the collection of the supernatant. The C-dots and medication samples were subjected to analysis by measuring their absorbance at wavelengths of 242 nm and 210 nm, respectively. The drug entrapment was quantified using the following mathematical equation:[19-22]

$$\text{Drug entrapment} = \frac{\text{drug amount} - \text{drug in supernatant}}{\text{drug amount}} \times 100$$

Scanning Electron Microscopy (SEM)

SEM was used to visualize the shape and surface morphology of loaded NCs. SEM images were taken at different magnifications of 2000x and 3500x and expressed in Figure 1.

Electrophoresis Studies of C-dots

To get an idea about the charge over C-dots, a gel electrophoresis study was performed.[20] The particles move through the cell according to their surface charge and polarity.

Ex vivo Permeation Study

The goat's ocular organs were selected as the focus of the *ex vivo* permeation study. The experiment utilized a modified Franz diffusion cell. The procurement of goat eyes occurred from a butcher shop, followed by preservation in a standard saline solution at a concentration of 0.9% w/v. The preservation process occurred at a temperature of 4°C. All research was performed in a sterile environment. The eyes were meticulously cleaned with PBS and subsequently scrubbed to eliminate any residual debris. The cleansed cornea was positioned in the center area of both the donor and recipient compartments of the diffusion cell. The corneal exposure area was measured at 1.5 cm. The lower container held an adequate volume of freshly made buffer solution. Subsequently, 1 mL of the samples was retrieved from the bottom compartment after penetrating the cornea, originating from the donor compartment. The experiment was performed at a temperature of 37°C, with a rotational speed set at 50 revolutions per minute. The samples were collected from the acceptor compartment at consistent time intervals, each with a volume of 1 mL. The sample collection began 10 min after the experiment commenced and continued for 1 hr. Samples were extracted at consistent intervals of 10 min, while the sink condition was perpetually upheld. Time Vs percentage drug release from NCs at goat eye were recorded at 210 nm. It is expressed in Figure 2.

Hydration Study of Cornea

The purpose of this study was to evaluate the moisture levels of corneas treated with clonidine hydrochloride NCs loaded with carbon dots. The cornea of the goat was immersed in NCs and the weight of the cornea was measured while it was still wet. The cornea that had been bathed was afterward placed in a hot air oven set at a temperature of 60°C for duration of 3 days. The dry weight was recorded after a period of three days and the level of corneal hydration was determined using the following equation:

$$\% \text{ Corneal Hydration} = \frac{\text{Wet Wt. of Cornea} - \text{Dry Wt. of Cornea}}{\text{Dry weight of Cornea}} \times 100$$

In vivo Pharmacodynamics Study for Intraocular Pressure Measurement

The nanocarriers loaded with a drug were assessed for their efficacy in lowering Intraocular Pressure (IOP) in New Zealand rabbits weighing between 2.5 and 3.5 kg. The rabbits were chosen for their white appearance, and glaucoma was induced in them for the study. The samples were amended for 7 days at a temperature of 25±1°C, with relative humidity maintained at 50±10%. The rabbits had full access to food and water and the animals underwent the induction of glaucoma using a steroid model. The research was authorized by the Animal Ethical Committee of the Shambhunath Institute of Pharmacy Jhalwa, Prayagraj (IAEC). The research was designated the protocol number SIP-IAEC/012/05/22. The animals were categorized into three groups, each comprising 6 rabbits. Group I received the marketed formulation, while Group II animals were administered the loaded NCs. Group III was selected as the control group. Intraocular Pressure (IOP) was measured at various intervals using the widely recognized Schiotz tonometer. The conjunctival sac of the left eye of a rabbit was treated with a commercially available formulation and 50 µL of 0.1% clonidine (1 mg/mL) loaded nanocarriers. The Intraocular Pressure (IOP) was measured at various time intervals for all the formulations and shown in Figure 3, using the right eye as the control. The equation presented below is employed to calculate the percentage decrease in IOP.

$$\% \text{ decrease in IOP} = \frac{IOP\ control\ eye - IOP\ control\ eye}{2}$$

Irritation Test of Eye

The ocular irritation test was performed in accordance with Test Guideline 405 as forth by the Organization for Economic Cooperation and Development (OECD). A particular breed of White New Zealand rabbits, distinguished by their weight range of 2.5-3.5 kg, was selected to examine discomfort associated with loaded NCs. Three animals were selected for participation in the investigation. The animals were kept in ambient conditions, with a temperature of 25±1°C and a relative humidity of 50±10%. During the trial, a regular 12 hr cycle of illumination and obscurity was maintained, while the animals were supplied with standard laboratory rations to meet their nutritional needs. During the whole research, a sufficient quantity of potable water was consistently supplied. Nanoparticles (NCs) and commercially available formulations were delivered to the conjunctiva of the left eye of rabbits in a volume of 50 µL containing 0.1% clonidine (1 mg/mL). The right eye was designated as the control group. The ocular structures of the rabbit were analyzed at four distinct time intervals: 1 hr, 24 hr, 48 hr and 72 hr. The study was concluded if no signs of pain were detected after 72 hr duration. The animals had a three-day examination at various intervals to assess eye irritation, redness, lesions, corneal ulceration and other associated problems. The experiments were conducted in duplicate and the results are shown in Figure 4.

RESULTS

In vitro Study

Various research organizations around have reported combination therapy as a feasible solution for treating resistant bacterial infections. Nanoscale bactericidal agents have garnered considerable attention due to their ability to impede bacterial resistance development. As a constituent of the combined therapy, C-dots were synthesized utilizing para-hydroxy acetanilide, commonly known as paracetamol, which is an anti-pyretic and analgesic medication, as the carbon source. In this study, a rapid heating approach utilizing microwaves was utilized to produce luminous Carbon-dots. The formation of Carbon-dots was seen through their distinct blue luminescence, which was clearly visible when exposed to UV irradiation. The literature reports the presence of synthesized C-dots with absorbance maxima observed at 243 nm and 266 nm, which may be attributed to the π-π^* and n-π^* transitions. The aforementioned materials exhibited a luminescence peak at a wavelength of 450 nm when subjected to Ultraviolet (UV) light[23-25] with a wavelength of 320 nm.

The gel electrophoresis analysis revealed that the C-dots exhibited a migration towards the positively charged electrode, indicating a negative surface charge. Previous research, including our own, has shown that Carbon dots (C-dots) had significant bactericidal properties against both Gram-positive and Gram-negative microbes. The current carbon dots (C-dots) also exhibited a reduction in bacterial cell proliferation when the dosage of C-dots increased. The objective of our study is to investigate the potential of co-administering C-dots[26] in conjunction with drug as a therapeutic approach for the management of glaucoma. Polymeric nanocarriers were designed to facilitate the simultaneous delivery of both C-dots and medicine within a single module.

Ex vivo Permeation and Corneal Hydration Study

Three drug samples that underwent permeation were collected at different time intervals and quantified using UV spectroscopy at a wavelength of 210 nm. Figure 2 presents a graph that illustrates the average permeation study, notably displaying the correlation

between the percentage of drug release and the time in minutes. The graph indicates that a substantial 90% of drugs demonstrate release within a 60 min period when delivered via loaded nanocarriers.

Pharmacodynamic Studies for Intraocular Pressure Measurement

The efficacy of loaded nanocarriers in treating glaucoma was compared to that of a typical formulation available in the market as eye drops. The decrease in intraocular pressure was assessed at regular intervals. The optical antihypertensive effect was determined by calculating and reporting the mean intraocular pressure for both the control and nanocarrier-treated eyes using tonometer (Figure 3). A study found a mean difference in Intraocular Pressure (IOP) of 1.9±2.1 mmHg at 1 hr following the administration of a standard formulation eye-drop. Subsequently, the IOP swiftly decreased to a value of 17.0±2.56 mmHg at the 8 hr mark. The formulated test samples, specifically the loaded Nanocarriers (NCs), exhibited a considerable decrease in Intraocular Pressure (IOP) up to 1 hr. Subsequently, a significant reduction in IOP was observed. The measured value was determined to be 14.3±2.22 mm Hg at the 8 hr mark, as depicted in Figure 3.

Irritation Test of Eye

The loaded nanocarriers were applied topically to the ocular region of the experimental model, namely the left eye of Albino rabbits. The animals were thereafter observed for three days to evaluate the level of red pigmentation. The zero point on the scale was assigned to denote compounds that are neither irritating nor corrosive. Supplementary rabbits were incorporated into the testing procedure to corroborate and authenticate the acquired results. The study results demonstrate that no eye injuries were recorded in any of the animals throughout duration of three days (Figure 4).

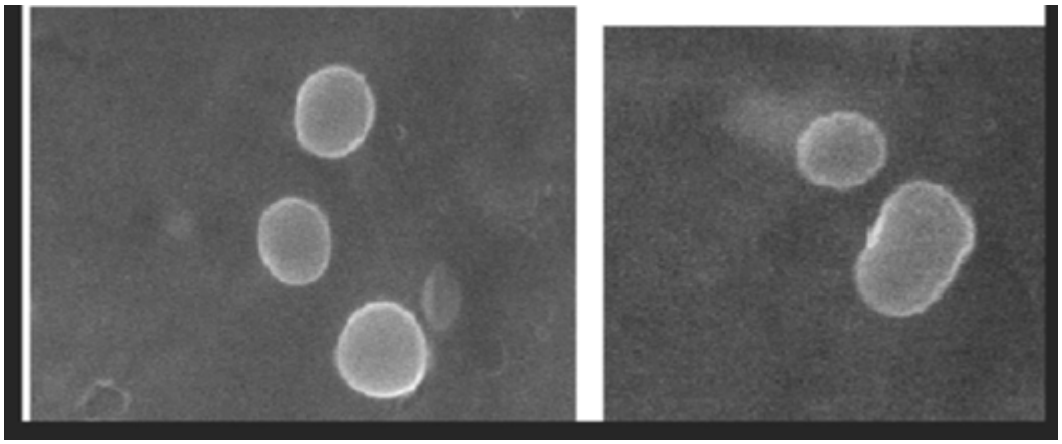

Figure 1: SEM of clonidine and C-dots loaded nanocarriers.

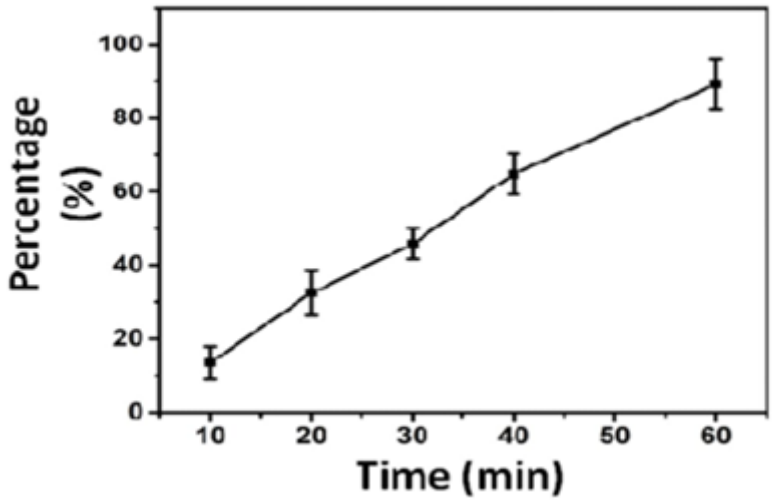

Figure 2: Time Vs percentage drug release from NCs at goat eye (Mean±SD, *n*=3).

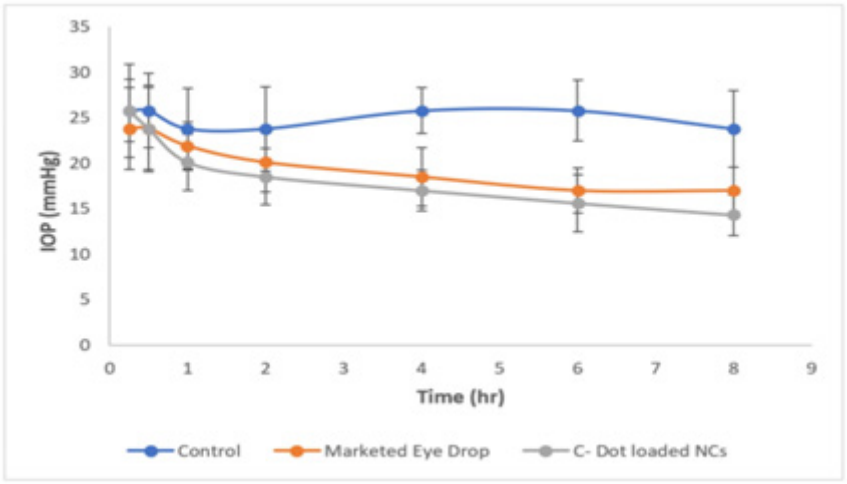

Figure 3: *In vivo* Pharmacodynamic study of different formulations.

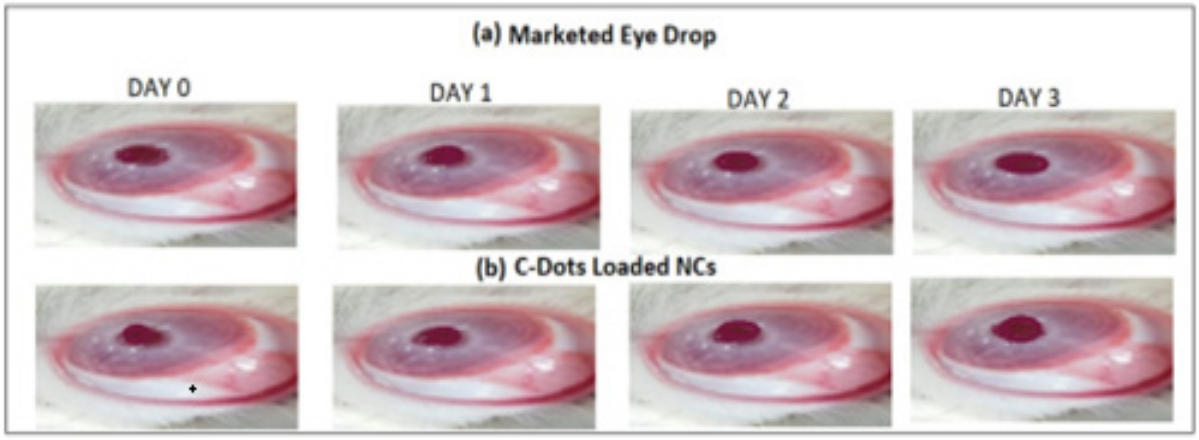

Figure 4: Irritation test over rabbit eyes treated with 100 µL of (a) Marketed Eye Drop (0.1%) and (b) C-Dots Loaded NCs.

DISCUSSION

The nanocarriers were observed using scanning electron microscopy, revealing that the majority of the NCs had a spherical morphology with smooth surfaces. The mean diameter of the Nanoparticles (NCs) was determined to be 125 nm. Previous investigations have established that size is adequate for ocular delivery.[27-29] The nanocarriers demonstrated a high drug loading efficiency, with approximately 75.3% of the drug encapsulated by them. The hydration test is an effective technique for evaluating eye damage. The use of clonidine hydrochloride and C-dots loaded nanocarriers has demonstrated a significant enhancement in corneal surface hydration. The corneal hydration percentage observed was 78%.

The observed value shows that the inclusion of loaded nanocarriers has exhibited beneficial hydration capabilities, leading to improved medication bioavailability. Nanocarriers enhance the efficacy and precision of drug delivery. The control group recorded an initial Intraocular Pressure (IOP) of 25.8±3.45 mmHg, which dropped to 23.8±4.22 mmHg after 8 hr of observation. The study results demonstrated that the decrease in Intraocular Pressure (IOP) was more significant in the group administered the present loaded nanocarriers than in the control group. The decrease in Intraocular Pressure (IOP) attained with the current loaded nanocarriers was comparable to that of the commercial product. The results of our investigation demonstrate a more significant decrease in intraocular pressure when utilizing loaded nanocarriers in comparison to commercially available options. Following a thirty min interval, a reduction in Intraocular Pressure (IOP) was noted, with a measured value of 2.0±0.61 mmHg, in the presence of loaded Nanocarriers (NCs). The anti-glaucomatic effect of NCs has been shown to last for 8 hr, with a statistical significance of $p<0.01$. A persistent reduction in intraocular pressure, averaging 14.3±2.22 mmHg, was observed after this length.

The reduction in IOP was more pronounced with loaded nanocarriers than with the marketed formulation over an 8 hr period, yielding a statistically significant p-value of less than 0.01. The experimental results unequivocally demonstrate that the assessed nanocarriers provide a substantial decrease in

intraocular pressure over an extended period, in contrast to the conventional eye drop formulations now available. The standard formulation of eye drops on the market is hindered by a limitation: its low viscosity restricts prolonged adherence to the cul-de-sac. In contrast, our experimental formulation (designated as NCs) demonstrates enhanced residence time on the ocular surface, facilitating a prolonged release of the encapsulated medication and so extending the period of therapeutic efficacy. The non-corrosive and non-irritating properties of our NCs have been established. It can be utilized safely for ophthalmic applications.

CONCLUSION

A combination therapy of C-dots and clonidine was attempted to manage glaucoma efficiently. The polymeric NC variant has exhibited considerable bactericidal efficacy in prior research. The delivery of Clonidine Hydrochloride was conducted simultaneously and laboratory results demonstrate that the NCs displayed a spherical morphology. The spherical form has been shown to be beneficial for ocular medication administration, as evidenced by several *in vitro, ex vivo* and *in vivo* studies. *Ex vivo* studies have shown that drug-loaded nanocarriers provide efficient drug release, rendering them appropriate for ocular delivery. Furthermore, in *in vivo* tests, it has been observed that these loaded nanocarriers release the medication in a manner that facilitates superior drug delivery to the ocular surface. Moreover, the drug's release can be regulated over a prolonged period. The extension of medicine retention on the cornea is improved, leading to a prolonged therapeutic impact. Therefore, it is proposed that the existing co-administration strategy may be suitable for the simultaneous management of glaucoma, secondary bacterial infection and extended ocular medication release.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS APPROVAL

The study was permitted by Animal Ethical Committee of Institute (IAEC), Shambhunath Institute of Pharmacy Jhalwa, Prayagraj with the protocol no. (SIP-IAEC/012/05/22).

ABBREVIATIONS

NCs: Nanocarriers; **GQDs:** Graphene Quantum Dots; **C-Dots:** Carbon Dots; **CH:** Clonidine Hydrochloride; **IOP:** Intra Ocular Pressure; **PEG:** Polyethylene Glycol; **PBS:** Phosphate Buffer Saline; **SEM:** Scanning Electron Microscopy.

SUMMARY

The study focuses on the use of NCs for ocular delivery, revealing their spherical morphology and smooth surfaces. The mean diameter of NCs was 125 nm, which is adequate for ocular delivery. The nanocarriers showed high drug loading efficiency, with 75.3% of the drug entrapment efficiency. The hydration test, a method for assessing ocular injury, showed a notable increase in hydration at the cornea's surface. The study also found that loaded nanocarriers have favorable hydration properties, resulting in enhanced drug bioavailability. The study also found a greater reduction in IOP when using loaded nanocarriers compared to commercially available alternatives. The anti-glaucomatic impact of NCs was documented to persist for 8 hr, with a consistent decrease in intraocular pressure. The percentage decrease in IOP exhibited a larger magnitude in the case of loaded nanocarriers compared to the marketed formulation. The non-corrosive and non-irritating character of NCs has been demonstrated, making it safe for ocular purposes.

REFERENCES

1. Parveen S, Shukla N, Shivalkar S, Sahoo AK, Bhatt N. A Combination Therapy of C-Dots and Clonidine Hydrochloride Loaded Nanocarriers for Ocular Drug Delivery: Formulation, Characterization and *ex vivo* Evaluation. Eur. Chem. Bull. 2023; 12;8: 2020-32.
2. Shivalkar S, Chowdhary P, Afshan T, *et al.* Nanoengineering of biohybrid micro/nanobots for programmed biomedical applications. Colloids and Surfaces B: Biointerfaces 2023; 222: 113054.
3. Gautam PK, Shivalkar S, Singh A, *et al.* (9783527834143): Bio-inspired Nanocomposites for Remediation of Pharmaceutical Pollutants. Nanotechnology for Environmental Remediation, 2022
4. Megan M., Elle B, *et al.* Considerations for polymer used in ocular drug delivery. Frontiers in medicine 2022; 8: 787644
5. Raid G, Alany, Ali N. Eudragit L100/Polyvinyl Alcohol Nanoparticles Impregnated Mucoadhesive Films as Ocular Inserts for Controlled Delivery of Erythromycin, Development, Characterization and *In vivo* Evaluation. MDPI Biomedicines 2022; 10: 1-19
6. Shivalkar S, Arshad F, Sahoo AK, *et al.* Visible Light-Mediated Photoactivated Sulfur Quantum Dots as Heightened Antibacterial Agents. ACS Omega 2022; 20; 7;37: 33358-64
7. Engy A, Abdel A, Elkheshen S A, *et al.* Augmented *in vitro* and *in vivo* profiles of brimonidine tartrate using Gelatinised core Liposome. International Journal of Nanomedicine 2022; 17: 2753-76
8. Shivalkar S, Singh V, Sahoo AK, *et al.* (9780128203187): Bioremediation: a potential ecological tool for waste management. Bioremediation for Environmental Sustainability, 2021: 1-21
9. Shivalkar S, Verma A, Singh V, *et al* (9781119769897): Dermatological Delivery of Nanodrugs, Applications, Toxicity and Safety. Nanotechnology in Medicine: Toxicity and Safety, 2021
10. Srividya G, Tejashree W. Nanocarriers for ocular drug delivery: current status and translational opportunity. Royal society of Chemistry 2020; 10: 27835-55
11. Shivalkar S, Gautam PK, Verma A, *et al.* Autonomous magnetic microbots for environmental remediation developed by organic waste derived carbon dots. Journal of Environmental Management 2021; 297: 113322
12. Pengfei Z, Jiachen S, *et al.* Assembly of carbon dots into frameworks with enhanced stability and antibacterial activity. Nanoscale Research Letters 2021: 1-10
13. Shivalkar S, Sahoo AK (978-0-7354-2395-4): Bio-Molecules Sensing Using Physical and Microfluidics Devices. MEMS application in biology and healthcare, 2021: 6-1-6-36

14. Astrid S, Del AEM, Korzhikov VIV, *et al.* Design principles of ocular drug delivery systems: importance of drug payload, release rate and material properties. Drug Discovery Today 2019; 24;8: 1446-57
15. Chauhan MK, Khanna G. Recent advance of nanotechnology for the treatment of glaucoma disease. World Journal of Pharmaceutical Research 2018; 1;15: 239-57
16. Nida P, Singh S. Lipoidal Nanoparticulate Drug Delivery of Ofloxacin for Ocular use. World Journal of Pharmaceutical Research 2018; 7;1: 1006-25
17. Sara S, Jaleh B, Barzegar JM, *et al.* Formulation and Evaluation of Eudragit RL-100 Nanoparticles Loaded *In Situ* Forming Gel for Intranasal Delivery of Rivastigmine. Advanced Pharmaceutical Bulletin 2020; 10;1: 20-9
18. Jamal GS, Ameeduzzafar Z, Chandra K, *et al.* Clarithromycin, loaded ocular chitosan nanoparticle formulation, optimization, characterization, ocular irritation and antimicrobial activity. International Journal of Nanomedicine 2020; 15: 7861-15
19. Sonia D, Govind A, Singh RV, Thakur G. Recent advances in nano formulations for ophthalmic drug delivery. Journal of Pharmaceutical Sciences and research 2020; 12;1: 213-23
20. Clotide J, Shima G, Nasim A, Reza D. Advances and limitation of drug delivery system formulated as eye drops. Journal of controlled release 2020; 321: 1-22
21. Kaushal K, Mohd F, Nida P. Preparation and Evaluation of Ocuserts for Increasing the Bioavailability of an Antifungal Drugs. Acta Scientific Pharmaceutical Sciences 2020; 6: 17-23
22. Reddy PN, Bhaskar K. Spectrophotometric determination of drugs and pharmaceuticals by using folin-ciocalteu reagent. International Journal of Research and Analytical Reviews 2020; 7: 1
23. Abhishek S, Suresh K, Preeti K, Verma VK. PLGA nanoparticles for ocular delivery of loteprednol etabonate: A corneal penetration study, Artificial cells. Nanomedicine and Biotechnology 2017; 45;6: 1156-64
24. Sukhbir S, Arora S, Paul SY, Neelam. An overview of multifaceted significance of Eudragit polymers in drug delivery systems. Asian J Pharm Clin Res 2015; 8;5: 1-6
25. Katpale T, Avinash, Shinde A. Formulation and evaluation of Thermo reversible *in situ* ocular gel of Clonidine hydrochloride for glaucoma pharmacophore 2015; 6;5: 220-32
26. Xu X, Zhang K, Zhao L, *et al.* Aspirin-Based Carbon Dots, a Good Biocompatibility of Material Applied for Bioimaging and Anti-Inflammation. ACS Appl Mater Interfaces 2016; 7; 8;48: 32706-16
27. Youfu W, Aiguo H. Carbon quantum dots:synthesis, properties and applications. Journal of Material Chemistry C 2014; 6921-39
28. Swarnali D, Preeti K, Suresh, Deshmukh R. Design of Eudragit RL100 nanoparticle by nanoprecipitation method for ocular delivery. Nanomedicine: Nanotechnology Biology and Medicine 2010; 6: 318-23
29. Prabhu P, Kumar N, Koland M, *et al.* Preparation and evaluation of nanovesicles of brimonidine tartrate as an ocular drug delivery system. Journal of Young Pharmacists 2010; 2;4: 356-61

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