World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 5
Page: 798-809

NOVEL DRUG DELIVERY APPROACHES FOR CARBONIC ANHYDRASE INHIBITORS IN GLAUCOMA THERAPY

Sunil Saini*, Kamal Singh Rathore

Department of Pharmaceutics, Bhupal Nobles' College of Pharmacy, Udaipur (Raj) India 313001.

Article Received: 20 March 2026 | | ***Article Revised: 11 April 2026*** | | ***Article Accepted: 01 May 2026***

***Corresponding Author: Sunil Saini**
Department of Pharmaceutics, Bhupal Nobles' College of Pharmacy, Udaipur (Raj) India 313001.
DOI: https://doi.org/10.5281/zenodo.20234613

How to cite this Article: Sunil Saini, Kamal Singh Rathore (2026) NOVEL DRUG DELIVERY APPROACHES FOR CARBONIC ANHYDRASE INHIBITORS IN GLAUCOMA THERAPY. World Journal of Pharmaceutical Science and Research, 5(5), 798-809.

ABSTRACT

Glaucoma, a leading cause of irreversible blindness worldwide, is primarily associated with elevated intraocular pressure (IOP). Carbonic anhydrase inhibitors (CAIs), such as Dorzolamide and Acetazolamide, play a crucial role in reducing aqueous humor production. However, conventional formulations suffer from poor ocular bioavailability, rapid precorneal elimination, and low patient compliance. This review highlights recent advances in novel ocular drug delivery systems for CAIs, including nanoparticles, nanoemulsions, liposomes, dendrimers, and in-situ gelling systems. These approaches aim to overcome ocular barriers, enhance drug retention, and provide sustained release. The paper also discusses formulation challenges, clinical translation, and future perspectives in improving therapeutic outcomes for Glaucoma management.

KEYWORDS: Glaucoma, Carbonic Anhydrase Inhibitors, Ocular Drug Delivery, Nanoparticles, In-situ Gel, Bioavailability.

INTRODUCTION

Overview of Glaucoma

Glaucoma represents a heterogeneous group of progressive optic neuropathies characterized by structural damage to the optic nerve head and corresponding visual field loss. It is one of the leading causes of irreversible blindness globally, with a substantial and growing public health burden. According to recent analyses, the global prevalence of glaucoma is expected to increase significantly by 2050, particularly in developing countries such as India, where demographic expansion and aging populations contribute to rising incidence.Elevated intraocular pressure (IOP) remains the most important modifiable risk factor in glaucoma pathogenesis. Although glaucoma can occur with normal IOP (normal-tension glaucoma), numerous clinical studies highlight that IOP reduction is central to disease management and progression control. Clinical decision-making in glaucoma treatment is therefore heavily influenced by measured IOP

levels, alongside other factors such as optic nerve status and visual field changes. Glaucoma is broadly classified into primary and secondary types, with primary open-angle glaucoma (POAG) being the most common form, followed by angle-closure glaucoma. The disease is often asymptomatic in early stages, leading to delayed diagnosis and irreversible vision loss. Advances in diagnostic technologies and surgical innovations have improved disease detection and management; however, challenges remain in early diagnosis, patient adherence, and long-term therapeutic outcomes. Recent literature emphasizes that despite progress in pharmacological and surgical interventions, including minimally invasive glaucoma surgeries (MIGS), there is still a need for more effective, patient-friendly treatment approaches. In this context, pharmacotherapy—particularly agents that reduce aqueous humor production such as carbonic anhydrase inhibitors—continues to play a vital role.[1,2]

Role of IOP in disease progression

Intraocular pressure (IOP) is the most significant and well-established modifiable risk factor in the onset and progression of glaucoma. It represents the balance between aqueous humor production and its outflow through trabecular and uveoscleral pathways. Elevated IOP leads to mechanical and vascular stress on the optic nerve head, particularly at the lamina cribrosa, resulting in progressive retinal ganglion cell damage and irreversible visual field loss.

Sustained elevation of IOP contributes to structural deformation of the optic nerve head, impaired axoplasmic flow, and reduced ocular perfusion. These changes initiate a cascade of neurodegenerative events, including apoptosis of retinal ganglion cells. Clinical and epidemiological studies consistently demonstrate that higher baseline IOP is associated with increased risk of glaucoma development and faster disease progression.[3]

Importantly, even small reductions in IOP significantly decrease the risk of disease progression. Landmark clinical trials have shown that lowering IOP—regardless of the therapeutic modality—remains the cornerstone of glaucoma management. This applies not only to patients with elevated IOP but also to those with normal-tension glaucoma, where lowering IOP still slows disease advancement. IOP also plays a crucial role in clinical decision-making.

Treatment strategies, including pharmacological therapy, laser procedures, and surgical interventions, are primarily aimed at achieving a target IOP tailored to the severity and progression rate of the disease. However, fluctuations in IOP, both diurnal and long-term, have also been recognized as independent risk factors, emphasizing the need for sustained and controlled IOP reduction. Despite its central role, glaucoma progression can occur even at normal IOP levels, indicating the involvement of additional factors such as vascular dysregulation, genetic predisposition, and neurodegenerative mechanisms. Nevertheless, IOP reduction remains the only proven strategy to delay disease progression, highlighting its critical importance in both early and advanced stages of glaucoma. Schematic Representation of Aqueous Humour Flow and Carbonic Anhydrase Function in the Eye shown in figure 1.[4]

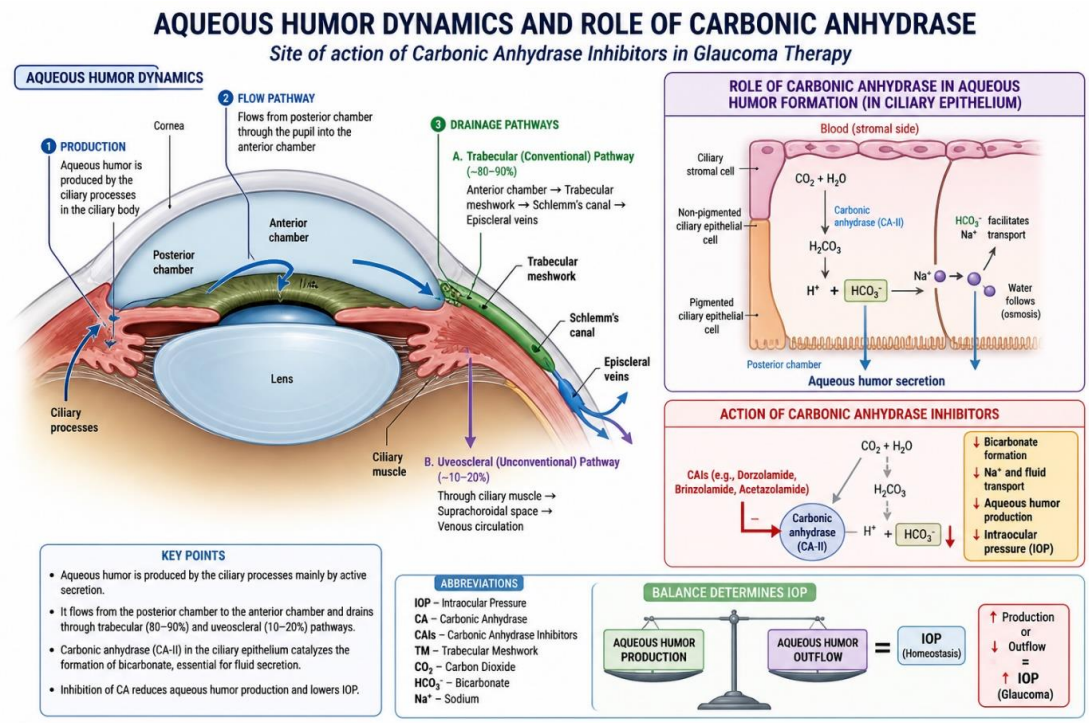

Figure 1: Schematic Representation of Aqueous Humour Flow and Carbonic Anhydrase Function in the Eye.

Importance of CAIs in therapy

Carbonic anhydrase inhibitors (CAIs) occupy a crucial position in glaucoma pharmacotherapy due to their ability to effectively reduce intraocular pressure (IOP), the primary modifiable risk factor for disease progression. By targeting aqueous humor production at the level of the ciliary epithelium, CAIs provide a well-established and mechanistically distinct approach to IOP control.One of the key therapeutic advantages of CAIs is their direct inhibition of aqueous humor secretion. By blocking carbonic anhydrase (primarily CA-II), these agents reduce bicarbonate ion formation, leading to decreased sodium and fluid transport into the posterior chamber. This ultimately results in a significant reduction in IOP, which is essential for slowing optic nerve damage and preserving vision.

CAIs are available in both topical and systemic formulations, enhancing their clinical versatility. Topical agents such as Dorzolamide and Brinzolamide are widely used for long-term management due to their localized action and reduced systemic side effects. In contrast, systemic agents like Acetazolamide are particularly valuable in acute situations, such as angle-closure glaucoma, where rapid IOP reduction is required.Another important aspect of CAIs is their role in combination therapy. They are frequently used alongside other antiglaucoma drugs (e.g., beta-blockers, prostaglandin analogs) to achieve additive or synergistic IOP-lowering effects. This is especially beneficial in patients who do not reach target IOP with monotherapy.

Despite these advantages, conventional CAI formulations face challenges such as limited ocular bioavailability, short duration of action, and the need for frequent dosing. These limitations can affect patient adherence and therapeutic outcomes. Consequently, there is a growing emphasis on developing novel drug delivery systems to enhance the efficacy and patient compliance of CAIs.Importantly, CAIs remain one of the few drug classes that specifically target aqueous humor production, complementing other therapies that primarily enhance outflow. This makes them an indispensable component of a comprehensive glaucoma treatment strategy.[5]

PHYSIOLOGY OF AQUEOUS HUMOR & ROLE OF CARBONIC ANHYDRASE

Aqueous humor production mechanism

Aqueous humor is continuously produced by the ciliary processes of the ciliary body through a combination of diffusion, ultrafiltration, and active secretion, with active secretion being the predominant mechanism. The process occurs across the bilayered ciliary epithelium, consisting of pigmented and non-pigmented epithelial cells, which function in a coordinated manner.

The production mechanism is primarily driven by ionic transport systems, including Na^+/K^+-ATPase pumps, bicarbonate transporters, and chloride channels. These transporters facilitate the movement of ions from the stromal blood supply into the posterior chamber. The osmotic gradient generated by ion transport promotes the passive movement of water, leading to aqueous humor formation. The newly formed aqueous humor flows from the posterior chamber through the pupil into the anterior chamber, where it maintains intraocular pressure (IOP) and supports metabolic functions of avascular tissues such as the cornea and lens.[6]

Role of carbonic anhydrase enzyme

Carbonic anhydrase (CA), particularly the CA-II isoenzyme, plays a pivotal role in aqueous humor secretion within the non-pigmented ciliary epithelium. This enzyme catalyzes the reversible hydration of carbon dioxide, generating bicarbonate ions that are essential for fluid transport.

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The generated bicarbonate ions (HCO_3^-) are co-transported with sodium ions (Na^+), facilitating osmotic water movement into the posterior chamber. This process significantly contributes to the rate of aqueous humor formation. Classical and contemporary studies have consistently demonstrated that inhibition of carbonic anhydrase leads to a marked reduction in aqueous humor secretion.[7,8]

Drug target relevance

Carbonic anhydrase represents a highly effective and validated pharmacological target in glaucoma therapy. Since aqueous humor production is a key determinant of IOP, inhibition of CA directly reduces fluid formation and thereby lowers intraocular pressure.

Clinically used carbonic anhydrase inhibitors, such as Dorzolamide and Acetazolamide, exert their therapeutic effect by blocking CA activity in the ciliary epithelium. This results in decreased bicarbonate production, reduced ionic transport, and diminished aqueous humor secretion.

The importance of CA as a drug target lies in:

- Direct modulation of aqueous humor production
- Proven efficacy in lowering IOP
- Utility in both acute and chronic glaucoma management
- Compatibility with combination therapy.[9]

CARBONIC ANHYDRASE INHIBITORS IN OPHTHALMOLOGY

Carbonic anhydrase inhibitors (CAIs) constitute an important class of antiglaucoma agents that exert their therapeutic effect by reducing aqueous humor production, thereby lowering intraocular pressure (IOP). Their clinical relevance in the management of Glaucoma has been well established, particularly as adjunctive therapy and in situations requiring rapid IOP control.

Classification and Drug Profile

CAIs are broadly categorized into topical and systemic agents based on their route of administration. Topical CAIs, including Dorzolamide and Brinzolamide, are commonly employed in long-term glaucoma management. Dorzolamide is typically formulated as a 2% ophthalmic solution and administered two to three times daily, whereas brinzolamide is available as a 1% suspension with a similar dosing frequency. Brinzolamide is often associated with improved ocular tolerability due to its near-physiological pH, while dorzolamide demonstrates higher aqueous solubility. Both agents are frequently used in fixed-dose combinations with other antiglaucoma drugs, enhancing therapeutic efficacy and patient compliance.

Systemic CAIs, most notably Acetazolamide, are administered orally or intravenously and are primarily reserved for acute clinical scenarios such as angle-closure glaucoma or preoperative IOP reduction. Acetazolamide exhibits potent inhibition of carbonic anhydrase activity, resulting in rapid and significant decreases in aqueous humor production. However, its systemic use is generally limited to short-term therapy due to a higher incidence of adverse effects.[10,11]

Mechanism of Action

The pharmacological action of CAIs is mediated through inhibition of carbonic anhydrase (predominantly the CA-II isoenzyme) localized in the non-pigmented ciliary epithelium. This enzyme catalyzes the reversible hydration of carbon dioxide, a reaction essential for bicarbonate ion formation:

CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-

Inhibition of this enzymatic process leads to decreased bicarbonate ion availability, subsequently reducing sodium and fluid transport into the posterior chamber. This results in diminished aqueous humor secretion and consequent lowering of IOP.[12]

Clinical Efficacy

Topical CAIs have demonstrated moderate efficacy in reducing IOP, typically achieving reductions in the range of 15–25%, making them suitable for chronic management of glaucoma and ocular hypertension. Their effectiveness is further enhanced when used in combination therapy, particularly in fixed-dose formulations such as dorzolamide/timolol and brinzolamide/brimonidine, which provide additive or synergistic IOP-lowering effects.

Systemic CAIs, particularly acetazolamide, are highly effective in achieving rapid IOP reduction and are therefore indispensable in acute glaucoma emergencies. Additionally, emerging evidence suggests a potential role of CAIs in the management of other ocular conditions such as macular edema, indicating broader therapeutic applications.

Limitations

Despite their clinical utility, CAIs are associated with several limitations. Topical formulations exhibit low ocular bioavailability due to rapid tear turnover, nasolacrimal drainage, and limited corneal permeability, necessitating frequent administration. Local adverse effects such as ocular irritation, burning sensation, blurred vision, and bitter taste are commonly reported. Rare hypersensitivity reactions, including blepharitis, have also been documented with topical agents.

Systemic CAIs, while effective, are associated with a higher incidence of adverse effects, including paresthesia, metabolic acidosis, electrolyte imbalance, and renal complications, which restrict their long-term use. Furthermore, frequent dosing regimens and discomfort associated with topical administration may compromise patient adherence. Molecular Structures of Key Carbonic Anhydrase Inhibitors in Glaucoma Therapy shown in figure 2.[13-15]

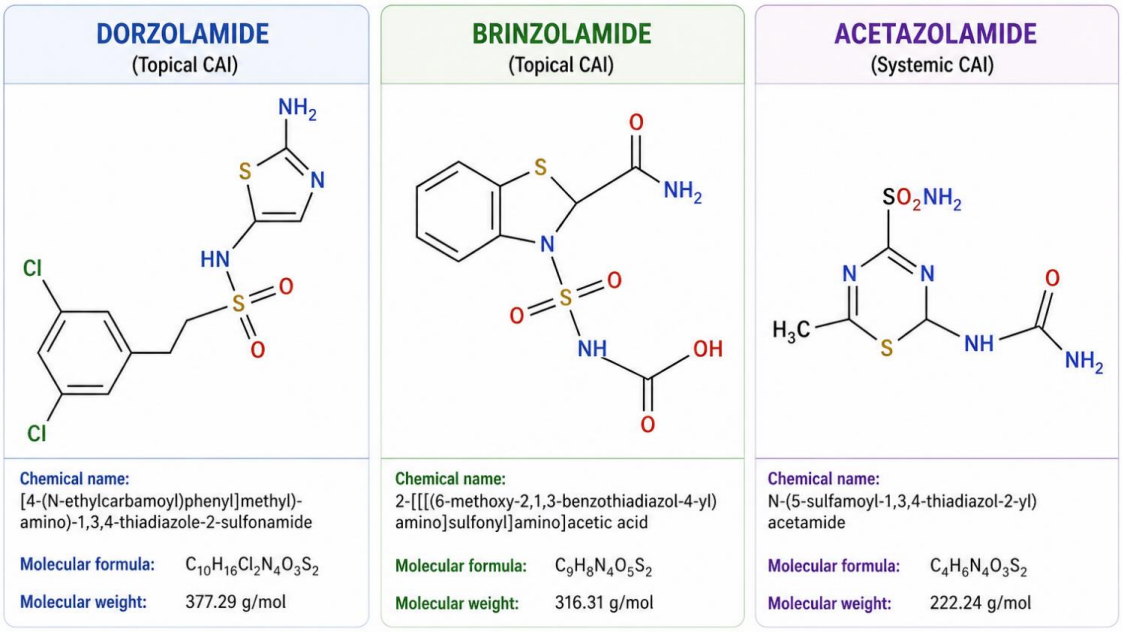

Figure 2: Molecular Structures of Key Carbonic Anhydrase Inhibitors in Glaucoma Therapy.

LIMITATIONS OF CONVENTIONAL OCULAR DELIVERY

Conventional ocular drug delivery systems, particularly eye drops, remain the most widely used approach for administering antiglaucoma agents, including carbonic anhydrase inhibitors. However, their therapeutic effectiveness is significantly limited by various anatomical, physiological, and formulation-related barriers. These limitations often result in poor ocular bioavailability and suboptimal clinical outcomes, thereby necessitating the development of advanced drug delivery strategies.

Tear Turnover

The precorneal tear film plays a critical role in ocular drug loss. Instilled formulations are rapidly diluted and eliminated due to continuous tear secretion and reflex blinking. Typically, the residence time of a drug in the precorneal area is only a few minutes, leading to the loss of a substantial portion of the administered dose. This rapid turnover significantly reduces drug absorption and limits therapeutic efficacy.

Nasolacrimal Drainage

A major fraction of topically administered drugs is drained through the nasolacrimal duct into the nasal cavity. This not only reduces ocular drug availability but also increases the risk of systemic absorption and associated side effects.

Consequently, only a small percentage of the administered dose reaches intraocular tissues, making conventional delivery highly inefficient.

Corneal Barrier

The cornea acts as a highly selective barrier to drug permeation due to its unique trilaminar structure, comprising the epithelium, stroma, and endothelium. The lipophilic epithelium restricts hydrophilic drugs, whereas the hydrophilic stroma limits lipophilic drug diffusion. This dual barrier significantly impedes drug penetration, resulting in low intraocular bioavailability.

Frequent Dosing and Poor Patient Compliance

Due to rapid drug elimination and limited ocular retention, conventional formulations require frequent administration to maintain therapeutic drug levels. This can lead to poor patient adherence, particularly in chronic conditions such as Glaucoma, where long-term treatment is essential. In addition, repeated dosing may increase the risk of local irritation and discomfort, further reducing compliance.[16]

NOVEL DRUG DELIVERY APPROACHES FOR CARBONIC ANHYDRASE INHIBITORS

The limitations associated with conventional ocular delivery systems—such as poor bioavailability, rapid precorneal elimination, and frequent dosing—have driven the development of advanced drug delivery platforms. Recent literature emphasizes that nanocarrier-based and stimuli-responsive systems can significantly enhance ocular drug retention, permeability, and therapeutic efficacy. These approaches are particularly relevant for improving the performance of carbonic anhydrase inhibitors in the management of Glaucoma.

Nanoparticles

Nanoparticles are submicron-sized carriers (10–1000 nm) that offer controlled and targeted drug delivery. They can be broadly classified into:

- Polymeric Nanoparticles

These are prepared using biodegradable polymers such as PLGA, chitosan, and Eudragit. Drugs may be encapsulated within the polymer matrix (nanospheres) or confined within a core surrounded by a polymer shell (nanocapsules).

- **Advantages**
  - Sustained and controlled drug release
  - Protection of drug from degradation
  - Enhanced corneal penetration
  - Mucoadhesive properties (especially with chitosan)

- **Relevance: Improve residence time and reduce dosing frequency of CAIs.**

Solid Lipid Nanoparticles (SLNs)

SLNs consist of solid lipid matrices stabilized by surfactants. They combine the advantages of liposomes and polymeric nanoparticles.

- **Advantages**:
  - High drug stability and biocompatibility
  - Controlled drug release
  - Improved ocular tolerance
- Limitations: Drug expulsion during storage and polymorphic transitions
- Recent Insight: Lipid composition and preparation methods significantly influence release profiles and stability.[17]

Liposomes

Liposomes are phospholipid-based vesicular systems composed of one or more lipid bilayers enclosing an aqueous core.

- Mechanism: Can encapsulate both hydrophilic and lipophilic drugs
- Advantages:
  - Biocompatibility and biodegradability
  - Enhanced drug retention at ocular surface
  - Reduced toxicity
- Application: Improve corneal permeation and sustain release of CAIs
- Limitation: Stability issues such as leakage and fusion[18]

Nanoemulsions

Nanoemulsions are thermodynamically stable dispersions of oil and water stabilized by surfactants, with droplet sizes typically in the nanometer range.

- Advantages:
  - Improved drug solubility (especially lipophilic drugs)
  - Enhanced permeability across corneal barrier
  - Increased bioavailability
- Additional Benefit: Better patient acceptability due to transparency and low viscosity
- Relevance: Suitable for delivering poorly soluble CAIs with enhanced therapeutic efficacy[19]

Dendrimers

Dendrimers are highly branched, tree-like macromolecules with a well-defined structure and multiple surface functional groups.

- Advantages:
  - Precise control over size and structure
  - High drug loading capacity
  - Targeted and controlled drug delivery
- Mechanism: Surface functionalization allows interaction with ocular tissues, enhancing drug retention
- Limitation: Potential cytotoxicity depending on surface charge[20]

In-situ Gels

In-situ gels are liquid formulations that undergo sol–gel transition upon instillation into the eye due to environmental triggers such as pH, temperature, or ionic strength.

- Types:
  - pH-triggered (e.g., carbopol-based)
  - Temperature-triggered (e.g., poloxamers)
  - Ion-activated systems
- Advantages:
  - Prolonged precorneal residence time
  - Sustained drug release
  - Reduced dosing frequency
- Relevance: Particularly promising for CAIs to overcome rapid tear washout[21]

Ocular Inserts and Implants

These are solid or semi-solid devices designed for controlled and sustained drug release.

- **Ocular Inserts**
- Placed in conjunctival sac
- Provide controlled drug delivery over extended periods
- Improve bioavailability and reduce systemic absorption

- **Ocular Implants**
- Surgically inserted devices for long-term drug release
- Suitable for chronic conditions requiring continuous therapy
- Offer precise and sustained drug delivery
- **Advantages**:
  - Eliminate need for frequent dosing
  - Improve patient compliance
  - Provide consistent therapeutic levels
- Limitations:
  - Invasive (implants)
  - Patient discomfort (inserts). Comparative table of novel ocular drug delivery systems shown in table 1.[22]

Table 1: Comparative Table of Novel Ocular Drug Delivery Systems.

Delivery System	Composition/Structure	Key Advantages	Limitations	Relevance for CAIs
Polymeric Nanoparticles	Biodegradable polymers (PLGA, chitosan)	Sustained release, mucoadhesion, improved corneal penetration	Possible polymer toxicity, scale-up issues	Enhances residence time and bioavailability
Solid Lipid Nanoparticles (SLNs)	Solid lipid core + surfactant	High stability, controlled release, good tolerability	Drug expulsion, polymorphic changes	Suitable for sustained delivery of CAIs
Liposomes	Phospholipid bilayer vesicles	Biocompatible, can carry hydrophilic &	Leakage, stability issues	Improves corneal permeation and

		lipophilic drugs, enhanced retention		reduces toxicity
Nanoemulsions	Oil-in-water nanosized droplets	Improved solubility, enhanced permeability, patient-friendly	Surfactant-related irritation	Ideal for poorly soluble CAIs
Dendrimers	Branched polymeric macromolecules	Targeted delivery, high drug loading, controlled release	Potential cytotoxicity	Enables precision delivery in ocular tissues
In-situ Gels	Stimuli-responsive polymers (pH/temp/ion)	Prolonged residence time, reduced dosing frequency	Viscosity-related discomfort	Overcomes tear washout of CAIs
Ocular Inserts	Solid/semi-solid devices	Sustained release, improved bioavailability	Patient discomfort	Reduces dosing frequency significantly
Ocular Implants	Biodegradable/non-biodegradable devices	Long-term controlled delivery, high precision	Invasive procedure	Suitable for chronic glaucoma therapy

FUTURE PERSPECTIVES

Advancements in the understanding of ocular physiology and drug delivery science are shaping the next generation of therapies involving carbonic anhydrase inhibitors (CAIs) for Glaucoma. Future perspectives focus on improving specificity, enhancing therapeutic outcomes, and integrating emerging technologies.

Isoform-Selective Carbonic Anhydrase Inhibitors

Carbonic anhydrase exists in multiple isoforms, among which CA-II and CA-IV are predominantly involved in aqueous humor production. Conventional CAIs inhibit multiple isoforms, which may contribute to off-target effects. Future research is directed toward the development of isoform-selective inhibitors that specifically target ocular isoenzymes.
Advantages:

- Increased therapeutic precision
- Reduced systemic and local side effects

Gene/Drug Hybrid Therapy

The integration of pharmacotherapy with gene-based approaches represents a promising frontier in glaucoma management. Gene therapy strategies aim to modulate the expression of proteins involved in aqueous humor dynamics, while CAIs can provide immediate pharmacological control.

Potential Approaches:

- Delivery of genes regulating aqueous humor outflow or production
- RNA-based silencing of carbonic anhydrase expression
- Combination of gene vectors with drug-loaded nanocarriers

AI-Based Formulation Design

Artificial intelligence (AI) and machine learning are increasingly being applied to pharmaceutical development, including ocular drug delivery systems.

Applications

- Prediction of drug–polymer interactions0
- Optimization of nanocarrier composition and size
- Simulation of drug release kinetics and ocular permeation
- Design of personalized treatment regimens[23-24]

CONCLUSION

Carbonic anhydrase inhibitors (CAIs) remain a cornerstone in the pharmacological management of Glaucoma due to their well-established ability to reduce aqueous humor production and lower intraocular pressure (IOP). Despite their clinical efficacy, conventional formulations are limited by poor ocular bioavailability, rapid precorneal elimination, and the need for frequent dosing, which can compromise therapeutic outcomes and patient adherence. Recent advancements in ocular drug delivery systems—including nanoparticles, liposomes, nanoemulsions, dendrimers, in-situ gels, and ocular inserts—have demonstrated significant potential in overcoming these limitations. These novel approaches enhance drug retention, improve corneal penetration, and enable sustained and targeted delivery, thereby optimizing the therapeutic performance of CAIs. Furthermore, emerging strategies such as isoform-selective inhibitors, gene–drug hybrid therapies, and AI-driven formulation design represent promising future directions that may redefine glaucoma treatment paradigms. Collectively, these innovations aim to improve efficacy, reduce side effects, and enhance patient compliance. In conclusion, the integration of advanced drug delivery technologies with a deeper understanding of ocular pharmacology holds great promise for improving the clinical utility of carbonic anhydrase inhibitors, ultimately contributing to more effective and patient-centric management of glaucoma.

REFERENCES

1. Saccà SC, Cutolo CA, Rossi T. Glaucoma: an overview. Handbook of Nutrition, Diet, and the Eye, 2019 Jan 1: 167-87.
2. Jayaram H, Kolko M, Friedman DS, Gazzard G. Glaucoma: now and beyond. The Lancet, 2023 Nov 11; 402(10414): 1788-801.
3. De Vitto C, Dattilo V, Virgili G, Fea AM, Garcia-Feijoo J, Azuara-Blanco A. The quality of reporting on Glaucoma Surgical Innovations during Early Development Stages using IDEAL Guidelines: a Systematic Review. Ophthalmology Glaucoma, 2026 Feb 4.
4. Polski A, Brintz BJ, Hess R, Kawamoto K, Medeiros FA, Stein JD, Stagg BC. Influence of intraocular pressure on clinical decision-making in glaucoma management. JAMA ophthalmology, 2026 Jan 8.
5. Jerrome S, Niranjana B, Joseph S, Swathi T, Kumaragurupari T, Senthilkumar VA, Krishnadas SR. Prevalence of Glaucoma in India over two decades and projections to 2050–A Systematic review and Meta-analysis. Ophthalmology Glaucoma, 2026 Jan 12.
6. Becker B. Carbonic anhydrase and the formation of aqueous humor: The Friedenwald Memorial Lecture. American journal of ophthalmology, 1959 Jan 1; 47(1): 342-61.
7. Sears ML, Sarrafpour S, Teng CC. Aqueous humor and the dynamics of its flow: Formation of aqueous humor. InAlbert and Jakobiec's Principles and Practice of Ophthalmology, 2022 Apr 23 (pp. 2561-2595). Cham: Springer International Publishing.
8. García-Llorca A, Carta F, Supuran CT, Eysteinsson T. Carbonic anhydrase, its inhibitors and vascular function. Frontiers in molecular biosciences, 2024 Jan 29; 11: 1338528.

9. Stamer WD, Kaufman PL, Delamere N. Production and flow of aqueous humor. Adler's Physiology of the Eye; Levin, LA, Kaufman, PL, Hartnett, ME, Adler, FH, Eds, 2024 Feb 14: 245-83.
10. Hallaj S, Shalaby WS, Sinha S, Myers JS, Razeghinejad R. Systemic Carbonic Anhydrase Inhibitors in Common Ophthalmic Diseases: A Scoping Review from A Clinical Standpoint. Current Ophthalmology Reports, 2025 Jul 8; 13(1): 9.
11. Stoner A, Harris A, Oddone F, Belamkar A, Verticchio Vercellin AC, Shin J, Januleviciene I, Siesky B. Topical carbonic anhydrase inhibitors and glaucoma in 2021: where do we stand?. British Journal of Ophthalmology, 2022 Oct; 106(10): 1332-7.
12. Giamello JD, Savioli G, Longhitano Y, Ferrari F, D'Agnano S, Esposito C, Tesauro M, Zanza C. The role of acetazolamide in critical care and emergency medicine. Journal of Geriatric Cardiology: JGC, 2024 Nov 28; 21(11): 1085.
13. Shahsuvaryan ML. Carbonic anhydrase inhibitors in the management of macular edema: a review of the literature. Medical Hypothesis, Discovery and Innovation in Ophthalmology, 2022 Apr 1; 11(1): 34.
14. Ayub F, Latif S, Latif H, Shah SA, Ali S, Yazar MQ. Dorzolamide/timolol and brinzolamide/brimonidine fixed combination topical drug therapy tn the management of intraocular pressure in primary open angle glaucoma. The Professional Medical Journal, 2025 Oct 2; 32(10): 1318-23.
15. Grozdanić S, Luzhetskii S, Lazić T, Milčić Matić N. Suspected dorzolamide–induced delayed hypersensitivity blepharitis in dogs. Acta Veterinaria, 2025; 75(4): 437-47.
16. Shadab S, Alam MA, Sharma PK, Paliwal D. Overcoming the therapeutic limitation of ocular drug delivery with the help of novel drug carriers. Current Nanomaterials, 2025 Mar; 10(1): 34-42.
17. Mohammed HA, Khan RA, Singh V, Yusuf M, Akhtar N, Sulaiman GM, Albukhaty S, Abdellatif AA, Khan M, Mohammed SA, Al-Subaiyel AM. Solid lipid nanoparticles for targeted natural and synthetic drugs delivery in high-incidence cancers, and other diseases: Roles of preparation methods, lipid composition, transitional stability, and release profiles in nanocarriers' development. Nanotechnology Reviews, 2023 Feb 18; 12(1): 20220517.
18. Akel H. *Development of lipid-and polymer-based nanocarriers for intranasal application* (Doctoral dissertation, University of Szeged (Hungary)).
19. Bajwa N, Mishra N, Jain NK, editors. Novel Drug Delivery Approaches: From Fundamentals to Advanced Carrier Systems. CRC Press, 2026 Mar 11.
20. Shaikh MA. Emerging Approaches in Novel Drug Delivery System.
21. Kumar M, Pathak D. A Comprehensive Review of Nanotechnology Based Nanoemulsion Delivery Systems for Targeted Drug Delivery and Enhanced Therapeutic Efficacy. Pharmaceutical Nanotechnology, 2025.
22. Adetuyi BO, Vega L. Advancements in Nanocarrier-Mediated Drug Delivery: Precision Strategies for Targeted Therapeutics and Improved Treatment Outcomes. InCancer Immunotherapy and Nanobiotechnology: An Interdisciplinary Approach, 2024 Jun 7 (pp. 673-757). Cham: Springer Nature Switzerland.
23. Hallaj S, Shalaby WS, Sinha S, Myers JS, Razeghinejad R. Systemic Carbonic Anhydrase Inhibitors in Common Ophthalmic Diseases: A Scoping Review from A Clinical Standpoint. Current Ophthalmology Reports, 2025 Jul 8; 13(1): 9.
24. Zulfiqar N, Asif MU, Ahmed A. Carbonic Anhydrase Inhibitors: Deciphering Pharmacological Mechanisms, Therapeutic Avenues, and Clinical Implications. Mathews Journal of Pharmaceutical Science, 2026 Jan 31; 10(1): 1-0.