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Research Article

Glaucoma And Rock Inhibitors: A Comprehensive Review

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ABSTRACT:
One of the main causes of permanent blindness, glaucoma is characterised by gradual damage to the optic nerve and is frequently linked to high intraocular pressure (IOP). While reducing IOP is the main goal of traditional therapy, recent studies have shown how important Rho-associated protein kinase (ROCK) is to the pathophysiology of glaucoma. There are various medication classes which are used in the treatment of glaucoma like Carbonic anhydrase inhibitors, Cholinergic agonist , α 2 - adrenergic agonists, β - adrenergic blockers, RHO kinase (ROCK), Inhibitors , Prostaglandin analogues, etc. Recent studies show increased use of ROCK inhibitors in a first line treatment as it acts directly on the root cause. This review focuses on the pathophysiology of glaucoma along with its types. This review also informs about available treatments for glaucoma (conventional and non-conventional) with a specific focus on the role of RHO kinase inhibitors along with the various drugs of this class. It also threw light on the available medical and surgical treatments. It also discussed various available conventional as well as non conventional ophthalmic dosage forms. This review prioritises on the new class of ROCK inhibitors, which includes ripasudil, fasudil and netarsudil. A brief about their mode of action, clinical studies, effectiveness, safety, and prospects for further research wete also discussed.

KEYWORDS: Glaucoma, ROCK inhibitors, ripasudil, netarsudil, intraocular pressure, optic nerve damage, aqueous humour dynamics,

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BACKGROUND:
Glaucoma is a leading cause of irreversible blindness worldwide, characterised by progressive optic nerve damage often associated with elevated intraocular pressure (IOP). It is a leading cause of irreversible blindness worldwide, affecting more than 80 million individuals.[1] The pathophysiology of glaucoma involves complex mechanisms, including impaired aqueous humour outflow, which can lead to retinal ganglion cell (RGC) death and visual field. [2],[3] Recent advancements in pharmacological treatments, particularly the use of Rho-associated kinase (ROCK) inhibitors, have shown promise in managing this condition [4],[5]

1. Introduction to Glaucoma

Glaucoma is a group of eye diseases characterized by progressive optic nerve damage, leading to irreversible vision loss primarily due to elevated IOP. The most common type is primary open-angle glaucoma (POAG), which is often asymptomatic until significant vision loss occurs. Other types include angle-closure glaucoma and normal-tension glaucoma. The pathophysiology of glaucoma involves the dysregulation of aqueous humor dynamics, leading to increased IOP, which can damage the optic nerve and result in visual impairment.[1]
It is a significant public health concern, affecting millions worldwide. This review presents a comprehensive overview of glaucoma, its

pathophysiology, and the emerging role of ROCK inhibitors in its treatment.

1.1. Types of Glaucoma

Glaucoma is defined by the presence of optic nerve damage, often associated with elevated intraocular pressure (IOP). The types of glaucoma are broadly classified based on the underlying mechanism of IOP elevation and the structural characteristics of the optic nerve: [2] [6]

- Open-angle glaucoma (OAG): The most common type, characterized by a wide drainage angle (the space between the iris and cornea). IOP elevation occurs due to impaired outflow of aqueous humor, the clear fluid that nourishes the eye. It is further classified into primary open-angle glaucoma (POAG), which is associated with no identifiable systemic disease, and secondary open-angle glaucoma (SOAG), which arises as a consequence of other eye conditions or systemic diseases.
- Angle-closure glaucoma (ACG): This type is characterized by a narrow drainage angle, leading to obstruction of aqueous humor outflow and rapid IOP elevation. It can be further categorized into primary angle-closure glaucoma (PACG) and secondary angle-closure glaucoma (SACG), depending on the underlying cause.
- Congenital glaucoma: A rare type that is present at birth, characterized by developmental abnormalities in the drainage angle.
- Normal-tension glaucoma (NTG): A type of glaucoma where optic nerve damage occurs despite IOP levels within the normal range. The exact underlying mechanisms are still under investigation, but it is thought to involve increased susceptibility of the optic nerve to damage, potentially due to reduced blood flow or other vascular factors.

Summary of traditional and modern classification of glaucoma is illustrated in figure 1. [9]

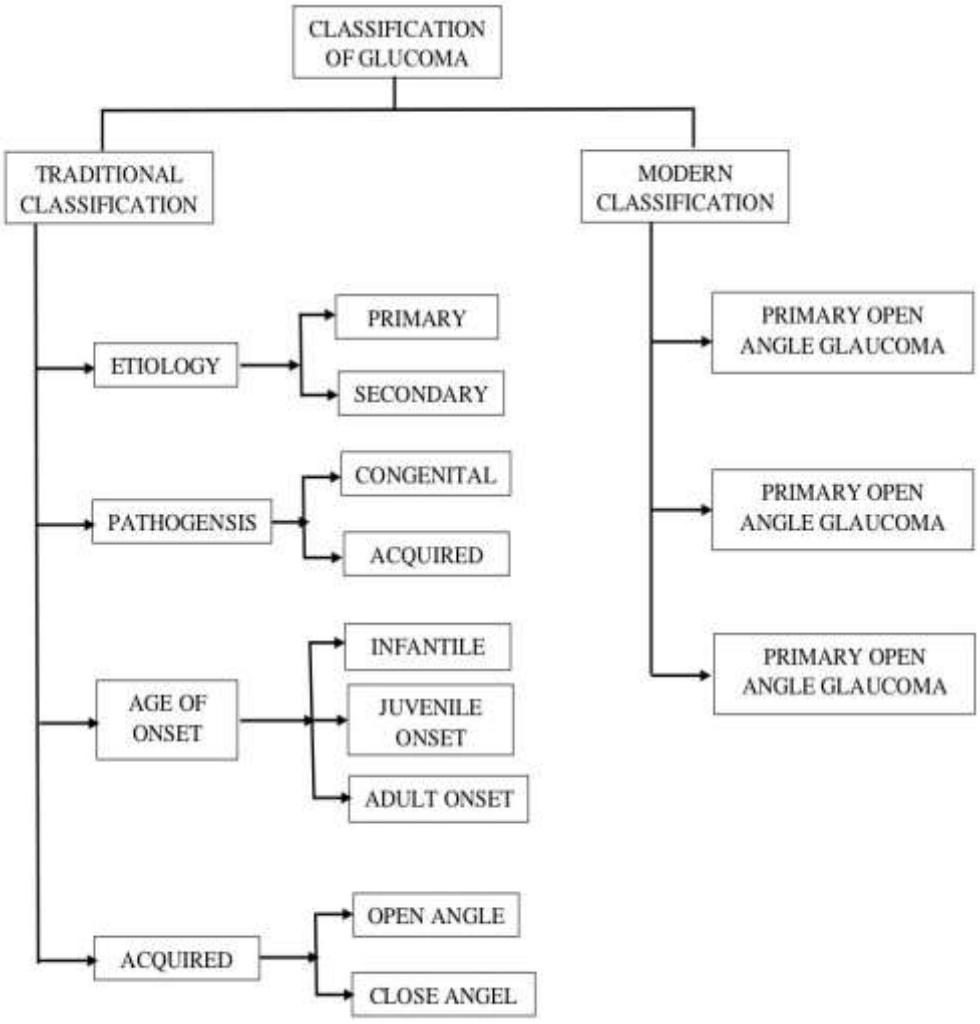


Figure 1: Classification of Glaucoma

1.2. Epidemiology and Risk Factors

Glaucoma is a significant public health burden, affecting millions globally. It is the second leading cause of blindness worldwide after cataracts. The prevalence of glaucoma increases with age, with individuals over 60 years old being at higher risk , with estimates suggesting

that by 2040, approximately 111.8 million individuals aged 40 to 80 will be affected globally [7] Key risk factors for developing glaucoma include age, family history, and elevated IOP. Specifically, age is a well-established risk factor, with studies indicating that the risk of glaucoma increases significantly in older populations [8] [9] Additionally, systemic conditions such as hypertension and diabetes have been linked to an increased risk of glaucoma, particularly primary open-angle glaucoma (POAG)[7] [8] Moreover, genetic predispositions play a critical role in glaucoma susceptibility. Genome-wide association studies have identified several genetic variants associated with glaucoma, emphasising the importance of hereditary factors in its pathogenesis .[10] Vascular risk factors, including impaired ocular blood flow and systemic vascular health, are also implicated in the development of glaucoma, particularly in normal-tension glaucoma (NTG) [11] [12] Some Risk factors for glaucoma include:

- ***Age:*** The risk of glaucoma increases significantly with age, particularly after 40 years old.
- ***Family history:*** A family history of glaucoma greatly increases the risk of developing the disease.
- ***Race/ethnicity:*** African Americans have a higher risk of developing glaucoma than Caucasians, and Hispanics are also at increased risk.
- ***High intraocular pressure (IOP):*** Elevated IOP is the primary risk factor for most forms of glaucoma. However, some individuals may develop glaucoma even with normal IOP.
- ***Myopia:*** People with nearsightedness (myopia) may be at increased risk of developing OAG and NTG.
- ***Certain medical conditions:*** Diabetes, hypertension, and systemic inflammation can increase the risk of developing glaucoma.
- ***Ocular trauma:*** Past eye injuries can increase the risk of developing glaucoma.
- ***Steroid use:*** Long-term use of steroid medications, either topically or systemically, can increase IOP and lead to glaucoma.

1.3 Pathophysiology of Glaucoma

1.3.1 Intraocular Pressure and Optic Nerve Damage

The pathophysiology of glaucoma is multifactorial and includes factors such as elevated IOP, vascular dysregulation, and neurodegenerative processes. Elevated IOP is primarily caused by an imbalance between the production and outflow of aqueous humor, with the trabecular meshwork playing a critical role in the maintenance of normal IOP levels. In POAG, structural and functional alterations within the trabecular meshwork contribute to outflow resistance, while in ACG, anatomical configurations lead to sudden increases in IOP.

The primary pathophysiological mechanism underlying most forms of glaucoma is elevated intraocular pressure (IOP). IOP is the pressure within the eye, maintained by the balance between the production and drainage of aqueous humor. Aqueous humor is a clear fluid that is constantly produced by the ciliary body, a structure in the eye. It flows through the anterior chamber (the space between the cornea and iris) and exits the eye through the trabecular meshwork, a network of tissue located at the angle between the iris and cornea. The chronic nature of the disease often results in a gradual loss of vision, making early detection and treatment critical [13] [15]

As shown in figure 2,[16] Elevated IOP damages the optic nerve, the bundle of nerve fibers that connect the eye to the brain. This optic nerve damage is responsible for the characteristic vision loss associated with glaucoma. Optic nerve damage occurs because elevated IOP compresses the optic nerve head, the point where the optic nerve fibers exit the eye. This compression can lead to axonal degeneration, the death of optic nerve fibers.

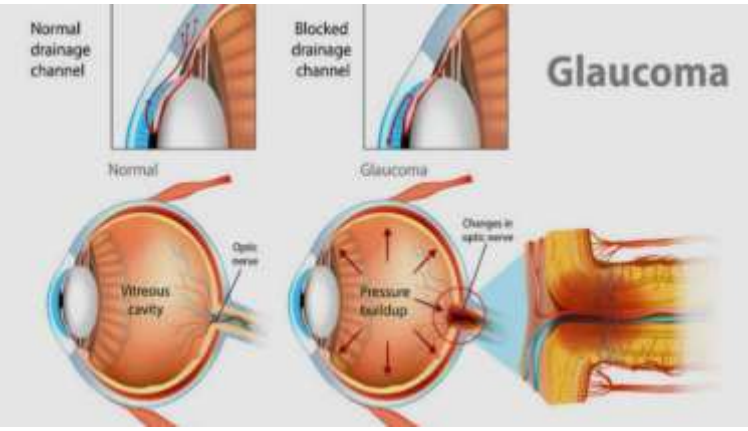


Figure 2: Pathophysiology of Glaucoma

1.3.2 The ROCK Signalling Pathway

Recent research has highlighted the role of Rho-associated protein kinase (ROCK) in the pathophysiology of glaucoma. ROCK is involved in various cellular processes, including smooth muscle contraction and cell motility, which are critical in regulating aqueous humor outflow through the trabecular meshwork [17] [18] ROCK functions as a downstream effector of the Rho GTPase signalling system, an essential mechanism that governs multiple cellular processes such as cell adhesion, migration, and cytoskeletal reorganisation. ROCK phosphorylates multiple downstream substrates, such as myosin light chain (MLC) and LIM kinases (LIMKs), upon activation by Rho GTPases, specifically RhoA. Dysregulation of ROCK signalling pathways has been implicated in

increased IOP and subsequent optic nerve damage, suggesting that ROCK inhibitors may offer therapeutic potential in managing glaucoma [17] [18]

- ***Phosphorylation of MLC:*** Actomyosin contraction is a result of ROCK-mediated MLC phosphorylation and is necessary for controlling cell shape, motility, and contractility. ROCK activation in the TM increases TM cell contraction, which increases resistance to aqueous humor outflow and raises IOP as a result.
- ***LIMK Phosphorylation:*** When LIMKs are phosphorylated by ROCK, cofilin, a protein that encourages actin depolymerization, is inhibited. This increases the amount of actin polymerization and encourages cytoskeletal contraction even more, which adds to the overall decrease in humor outflow.

Glaucoma is a multifaceted disease influenced by a combination of genetic, vascular, and mechanical factors. Elevated IOP remains the primary risk factor, but the involvement of ROCK signaling and other systemic conditions highlights the complexity of its pathophysiology. Understanding these interrelated factors is essential for developing effective prevention and treatment strategies for glaucoma.[17]

1.4 Medications and Surgical Interventions:

The primary goal of glaucoma treatment is to reduce IOP and prevent further optic nerve damage. Current medication treatment options are given in following table 1[19] [20]

Table 1: Medication

MEDICATION				
Category	**Drug**	**MOA**	**Dosage form**	**Marketed Formulation**
Carbonic anhydrase inhibitors	Dorzolamide	Inhibit carbonic anhydrase, an enzyme involved in aqueous humor production.	Nanoparticles, Nanoemulsion Liposomes, Microparticles, Niosomes, Implant, Inserts	Eye drops
	Brinzolamide	Inhibit carbonic anhydrase, an enzyme involved in aqueous humor production.	Nanoparticles, Nanocrystals, Liposomes, Nanocapsules, Nanoemulsion, Nanofibers, Implants	Eye drops
	Acetazolamide	Inhibit carbonic anhydrase, an enzyme involved in aqueous humor production.	Cubosomes, Spanlastics Transgelosomes, Implants, Niosomes, Bilosomes, Microsponges, Dendrimers	Eye drops
Cholinergic agonist	Pilocarpine	mimics the action of acetylcholine and activating muscarinic receptors which make some changes reduce intraocular pressure (IOP)	Nanoparticles, Nanocapsules, Dendrimers	Eye drops
α 2 - adrenergic agonists	Brimonidine	Reduce aqueous humor production and enhance outflow via the trabecular meshwork.	Nanoparticles, Inserts, Implant, Niosomes, Microspheres, Liposomes, Gelatin-core liposomes	Eye drops
RHO kinase (ROCK) Inhibitors	Ripasudil	Inhibit ROCK signaling, which promotes aqueous humor outflow and protects the optic nerve.	Solution	Eye drops
	Netarsudil	Inhibit ROCK signaling, which promotes aqueous humor outflow and protects the optic nerve.	Solution	Eye drops
	Fasudil	Inhibit ROCK signaling, which promotes aqueous humor outflow and protects the optic nerve.	Liposome, Microspheres	Eye drops
	Timolol	Reduce aqueous humor production by blocking beta-adrenergic receptors in the ciliary body.	Nanoparticles, Micelles, Cubosomes, Nanogel, Gelatinized	Eye drops

			core liposomes, Microemulsion	
β - adrenergic blockers	Levobunolol	Reduce aqueous humor production by blocking beta-adrenergic receptors in the ciliary body.	Nanoparticles, Microparticles	Eye drops
	Carteolol	Reduce aqueous humor production by blocking beta-adrenergic receptors in the ciliary body.	Nanocapsules, Nanoparticles, Chitosomes	Eye drops
	Metipranolol	Reduce aqueous humor production by blocking beta-adrenergic receptors in the ciliary body.	Nanocapsules	Eye drops
	Betaxolol	Reduce aqueous humor production by blocking beta-adrenergic receptors in the ciliary body.	Liposome, Nanoparticles, Niosones, Bilosomes	Eye drops
Prostaglandin analogues	Latanoprost	Enhance aqueous humor outflow via the uveoscleral pathway.	Nanoparticles, PEGylated solid, lipid, Micelles, Cubosomes, Nanoparticles	Eye drops
	Travoprost	Enhance aqueous humor outflow via the uveoscleral pathway.	Gold nanoparticles, Liposomes, Spanlastics, Nanoemulsion, Implants,	Eye drops
	Bimatoprost	Enhance aqueous humor outflow via the uveoscleral pathway.	Nanoparticles, Gold nanoparticles, Nanoparticle, Hydrogel, Microemulsion, Graphene oxide-laden Implants, Nanovesicular systems, Inserts	Eye drops
	Unoprostone	Enhance aqueous humor outflow via the uveoscleral pathway.	Transscleral device	Eye drops

Current treatment strategies for glaucoma primarily involve medications, laser treatments, and surgical interventions. Medications typically include topical eye drops such as prostaglandin analogs, beta-blockers, alpha agonists, and carbonic anhydrase inhibitors, which are administered daily to manage IOP [21] [22] [23] For instance, prostaglandin analogs are often prescribed at a dosage of one drop in the affected eye(s) once daily, while beta-blockers may be used twice daily [21] [22]. Laser treatments, such as selective laser trabeculoplasty (SLT), are also employed, particularly for patients who are non-compliant with medication [23] [24]

Surgical Interventions:

Interventions are considered when medications and laser therapies fail to adequately control IOP. Common surgical options include trabeculectomy, which creates a new drainage pathway for aqueous humor, and the implantation of drainage devices like the Ahmed glaucoma valve These procedures aim to enhance aqueous outflow and lower IOP effectively. [25] [26] Some of them are discussed below:

❖ ***Laser Trabeculoplasty:*** A laser procedure used to open the trabecular meshwork to improve aqueous humor outflow.

❖ ***Cyclophotocoagulation:*** A laser procedure that destroys part of the ciliary body to reduce aqueous humor production.

❖ ***Trabeculectomy:*** A surgical procedure that creates a new drainage pathway for aqueous humor to exit the eye.

❖ ***Selective Laser Trabeculoplasty (SLT):*** Uses a precise laser to target and treat the trabecular meshwork.

❖ ***Drainage Implants:*** Small devices implanted in the eye to drain excess aqueous humor.

2. ROCK INHIBITORS

ROCK inhibitors are a novel class of glaucoma medications that target the ROCK signalling pathway. The Rho-associated protein kinases (ROCKs), also known as Rho-kinase, are serine/threonine kinases that play a crucial role in the regulation of various cellular functions, including cytoskeletal organisation, cell migration, proliferation, and apoptosis. ROCKs are activated by the small GTPase Rho, a member of the Ras superfamily of small GTPases. There are two major

isoforms of ROCK, ROCK1 and ROCK2, which are highly homologous and are involved in a wide range of cellular processes.When Rho is activated, it binds to and activates ROCK. ROCK, in turn, phosphorylates various downstream targets, including myosin light chain (MLC), which results in an increase in actomyosin contraction. [27] [28]

2.2 Mechanism of Action:

ROCK inhibitors represent a novel class of medications that target the Rho/ROCK signaling pathway, which plays a crucial role in regulating aqueous humor outflow and maintaining IOP The mechanism of action (MOA) involves the relaxation of the trabecular meshwork and increased outflow facility, thereby reducing IOP (Germano et al.; Futakuchi et al.). Currently, ripasudil is a prominent ROCK inhibitor available in topical formulation, administered as one drop in the affected eye(s) once or twice daily (Kusuhara et al. 809-814).[28] Recent research has shed light on the crucial role of Rho-associated protein kinase (ROCK) in glaucoma pathogenesis. ROCK is a serine/threonine protein kinase that belongs to the AGC (protein kinase A, protein kinase G, and protein kinase C) kinase family. ROCK signaling plays a crucial role in regulating diverse cellular functions, including cytoskeletal organisation, cell proliferation, and apoptosis. In the context of glaucoma, ROCK activation contributes to both elevated IOP and optic nerve damage.[27] [29]. Pictorial representation of the mechanism of ROCK Inhibitors are given in figure 3. [49]

ROCK signaling has been implicated in the regulation of aqueous humor outflow and IOP. ROCK signaling also plays a role in the pathogenesis of optic nerve damage in glaucoma. Specifically, ROCK activation has been shown to:

➢ ***Increase trabecular meshwork resistance:*** ROCK promotes actomyosin contraction and increased tension in the trabecular meshwork, leading to reduced outflow of aqueous humor.

➢ ***Promote ciliary muscle contraction:*** ROCK activation in the ciliary muscle can lead to muscle contraction, which can both decrease outflow of aqueous humor and increase its production. [29]

➢ ***Inhibit uveoscleral outflow:*** ROCK activation has been shown to reduce uveoscleral outflow, an alternative pathway for aqueous humor drainage.

➢ ***Promote axonal degeneration:*** ROCK contributes to axonal degeneration through various mechanisms, including activation of downstream signaling pathways that lead to cytoskeletal disruption and impaired axonal transport.

➢ ***Promote astrocyte activation:*** ROCK activation has been linked to astrocyte activation, which can contribute to optic nerve damage by contributing to microglial activation, inflammation, and scarring around the optic nerve head.

➢ ***Induce apoptosis in retinal ganglion cells:*** ROCK activation can trigger apoptosis (programmed cell death) in retinal ganglion cells, the neurons that are responsible for transmitting visual information from the eye to the brain. [28]

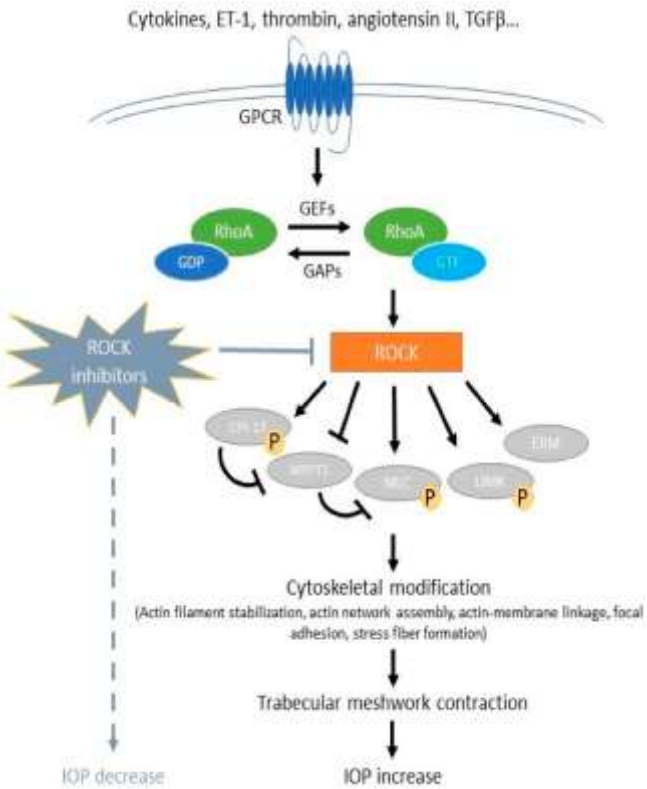


Figure 3: MOA of ROCK Inhibitors

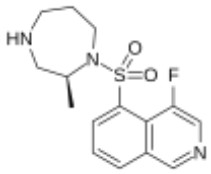
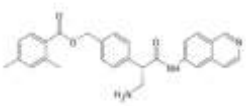
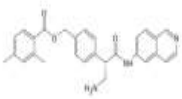
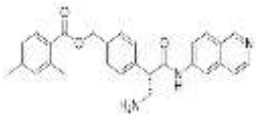
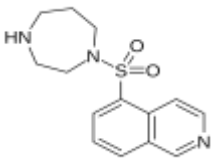
ROCK inhibitors like Ripasudil, Netarsudil, fasudil works by inhibiting this ROCK signalling has been shown to:

- **Enhanced trabecular meshwork outflow:** ROCK inhibitors decrease trabecular meshwork resistance by inhibiting actomyosin contraction. This improved outflow facilitates the drainage of aqueous humor, reducing IOP.
- **Increased uveoscleral outflow:** ROCK inhibitors may enhance aqueous humor outflow through the uveoscleral pathway, a secondary drainage route.
- **Reduced ciliary muscle contraction:** ROCK inhibitors may reduce ciliary muscle contraction, potentially decreasing aqueous humor production and contributing to IOP reduction. [29]

2.3 Drug profile of ROCK Inhibitors

ROCK inhibitors category includes drugs like Ripasudil Netarsudil, Fasudil, etc. Details about their structure, mechanism of action (MOA), also about their safety, efficacy and side effects are discussed in Table 2.[27] [28][29] [30] Clinical trials have demonstrated the efficacy of ROCK inhibitors in reducing IOP in various glaucoma types, including POAG and uveitic glaucoma.

Table 2: Drug Profile of ROCK Inhibitors

ROCK INHIBITORS				
Drug	**Structure**	**MOA**	**Side Effects**	**Efficacy**
Ripasudil		 Ripasudil is quinoline derivative, inhibits ROCK, a downstream effector of the Rho/RhoA kinase pathway. This inhibition results in vasodilation followed by increased outflow facility and ultimately reduced IOP.	 Common: Conjunctival Hyperemia, Headache, eye pruritus, blurred vision Potential: allergic reactions Retinal vein occlusion,	Clinical trials have demonstrated that ripasudil effectively lowers IOP in patients with open-angle glaucoma and ocular hypertension. Studies have reported a mean IOP reduction of 2-4 mmHg compared to placebo, especially significant in patients with uncontrolled IOP on other medications.
Netarsudil		Netarsudil, also belongs to quinoline derivative class, exerts its IOP-lowering effect by selectively inhibiting ROCK1. This ROCK1 isoform crucial for regulating trabecular meshwork function and outflow facility.	Common: Conjunctival Hyperemia, Blurred vision eye pruritus Potential: Rare, but may include allergic reactions	Similar to ripasudil, netarsudil has proven effective in lowering IOP. Trials have shown IOP reductions of 2-4 mmHg compared to placebo, supporting its use as a first-line therapy for glaucoma management.
Fasudil		Fasudil belongs to pyrimidine derivative class, inhibits both ROCK1 and ROCK2 isoforms. It has broader inhibition profile which contributes to its IOP-lowering effect by improving trabecular meshwork function and increasing uveoscleral outflow.	Common: Dizziness, Headache, hypotension flushing Potential: Further research needed to fully assess	While primarily used for treating cerebral vasospasm, fasudil has shown promise in treating glaucoma. Studies have reported a significant IOP reduction with fasudil, but further research is needed to establish its long-term efficacy and safety in glaucoma management.

These findings suggest that ROCK inhibitors may serve as effective adjunctive therapies in glaucoma management. The safety profile of ROCK inhibitors is generally favorable, with common side effects including conjunctival hyperemia and ocular discomfort Serious adverse events are rare, but ongoing monitoring is essential to ensure patient safety and treatment adherence.[30]

2.4 Key Studies and Findings

While compared with conventional glaucoma treatments, ROCK inhibitors present a viable substitute that has a number of benefits.

- **Targets the pathophysiology directly:** ROCK inhibitors specifically target the ROCK signaling system, which is important for controlling intraocular pressure and causing damage to the optic nerve. Conventional drugs frequently aim to reduce IOP via several means.
- **Possibility of neuroprotective effects:** ROCK inhibitors may possess qualities that shield the visual nerve from harm. This is a big help because the main goal of conventional glaucoma drugs is to lower IOP.
- **Single-agent therapy:** ROCK inhibitors provide the ease of a single-agent treatment plan by efficiently lowering IOP when used alone. For patients who have trouble adhering to intricate multi-drug regimens, this may be helpful.
- **Dose Reduction:** Patients respond better to the once-daily dosage schedule..
- **Safety Profile:** ROCK inhibitors show a distinct safety profile, suggesting potential advantages in patients who experience side effects from conventional treatments.
- **Efficacy**: ROCK inhibitors demonstrate comparable efficacy to traditional first-line therapies, with advantages particularly noted in certain populations.

However, there are some possible downsides linked with ROCK inhibitors:

- **High cost:** ROCK inhibitors are currently more expensive than certain conventional glaucoma treatments.
- **Lack of safety evidence:** Long-term safety evidence on ROCK inhibitors is currently inadequate, and further study is required to thoroughly examine their long-term consequences.
- **Not appropriate for all types of glaucoma**: While ROCK inhibitors have showed promise in the treatment of open-angle glaucoma, they may be ineffective in other types of glaucoma, such as angle-closure.

Compared to traditional glaucoma treatments, ROCK inhibitors offer a unique mechanism of action that may enhance patient outcomes. While conventional therapies primarily focus on reducing aqueous humor production or enhancing outflow, ROCK inhibitors directly target the cellular pathways involved in outflow regulation This novel approach may provide additional benefits, particularly for patients who are non-compliant with standard therapies. [27] [28] [29] [30]

2.5 . Future Scope in Potential Developments in ROCK Inhibitor Therapy

The future of glaucoma treatment rests on continued advancements in drug formulation, including:Even though ROCK inhibitors for the treatment of glaucoma have just recently been available, research is still being done to determine their potential and resolve their drawbacks:

- **Creating novel ROCK inhibitors:** Scientists are hard at work creating novel ROCK inhibitors that have enhanced pharmacodynamic profile, safety, and efficacy. Emerging technologies such as sustained-release implants and biodegradable polymers may revolutionise the management of glaucoma.
- **Examining the function of ROCK in different forms of glaucoma:** More study is required to determine the function of ROCK in diverse forms of glaucoma, including angle-closure and normal-tension glaucoma.
- **Analyzing the neuroprotective potential of ROCK inhibitors:** Research is being done in clinical trials to find out how neuroprotective ROCK inhibitors are, as well as whether they can stop or lessen damage to the optic nerve.
- **Investigating combination therapy:** In the future, researchers may look at the safety and effectiveness of mixing ROCK inhibitors with other glaucoma drugs to reach synergistic effects and improve outcomes. Pairing ROCK inhibitors with other classes of glaucoma medications to improve efficacy and compliance
- **Developing targeted ROCK inhibitors:** Researchers are exploring the possibility of developing more targeted ROCK inhibitors that specifically inhibit the ROCK isoforms involved in IOP regulation and optic nerve damage, minimizing off-target effects.
- **Personalised Medicine:** Understanding genetic and phenotypic variations among patients to tailor treatments effectively.

The future of glaucoma treatment may see the integration of ROCK inhibitors into combination therapies, potentially improving adherence and treatment efficacy. [27] Additionally, ongoing research into the neuroprotective effects of ROCK inhibitors may open new avenues for preserving retinal ganglion cells and preventing vision loss. [31] The development of sustained- release formulations and novel delivery systems could further enhance the therapeutic landscape for glaucoma management [30] [32]

CONCLUSION

While all three medicines significantly reduce IOP, their individual characteristics warrant careful study. Ripasudil and netarsudil, both specific ROCK inhibitors, have demonstrated efficacy and safety in glaucoma treatment. Their specific MOA and shown efficacy make them appealing therapeutic choices for both first-line and adjuvant therapy. Fasudil, with its broader ROCK inhibition profile, has intriguing potential but needs more research to establish its place in glaucoma treatment.

With their unique methods of action, ripasudil, netarsudil, and fasudil offer a substantial improvement in the treatment of glaucoma. While netarsudil and ripasudil have shown to be successful IOP-lowering medications, fasudil has encouraging potential but needs

more study to be sure it is safe and effective. ROCK inhibitors are predicted to change as the research landscape evolves

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