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Comparison of the impact of Ripasudil and Dorzolamide on intraocular pressure in patients on prostaglandin analogues

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This study reports on the effect of lowering intraocular pressure with the combination drug therapies, Ripasudil with Dorzolamide, given in conjunction with prostaglandin analogues (PGAs) in patients diagnosed with glaucoma. The study was conducted on a cohort of 120 glaucoma patients who required additional therapeutic interventions beyond latanoprost monotherapy to achieve optimal intraocular pressure (IOP) control. The IOP was measured weekly for 12 weeks during the study to evaluate the effectiveness of the drugs used in combination therapy. This compound, known as Ripasudil hydrochloride hydrate, or K-115, is a new class of Rho kinase inhibitors that have gained special interest because they decrease IOP without a well-characterised mechanism; its main advantage lies in enhancing aqueous outflow at the trabecular meshwork. The findings show that the IOP-controlling efficacy of Ripasudil is equal to that of Dorzolamide in combination therapy. In Group A, ocular discomfort was reported by 6 patients (10%), blurred vision by 3 patients (5%), and systemic side effects by 1 patient (1.7%). In Group B, ocular discomfort occurred in 4 patients (6.7%), and blurred vision occurred in 2 patients (3.3%), while no systemic adverse effects were reported. The overall incidence of adverse events was 16.7% in Group A and 10% in Group B, but this difference was not statistically significant ($P > 0.05$). This outcome underlines the role of Ripasudil as a potential substitute for patients who need supplementary IOP-lowering treatment over PGA monotherapy. In addition, the novel mechanism of Ripasudil presents some benefits, especially for patients with minimal response to carbonic anhydrase inhibitors. This study underscores the need to explore innovative adjunctive treatments for glaucoma and supports the clinical utility of Ripasudil as a safe and effective option when combined with prostaglandin analogues to achieve optimal IOP control.

Keywords: Ripasudil, Dorzolamide, Intraocular Pressure, Prostaglandin, Analogues

Glaucoma is a chronic, slowly progressive optic neuropathy that ranks as one of the major causes of irreversible blindness worldwide, next only to cataracts[1] and characterised by progressive loss of retinal ganglion cells, which leads to damage of the optic nerve as well as visual field defects. If untreated, glaucoma inevitably causes permanent loss of vision, with significantly impacting the quality of life in the patient[2]. Among its many forms, primary open-angle glaucoma is the most common in adults and is typically associated with increased intraocular pressure. However, glaucoma can occur even in the presence of normal intraocular pressure, suggesting a complex interplay of factors in its pathophysiology[3-5].

The reduction of intraocular pressure is the only identified modifiable risk factor for managing glaucoma. There have been many clinical studies that demonstrate that reducing IOP slows the progression of optic nerve damage and prevents further vision loss[6,7]. The methods used to reduce IOP include pharmacological therapy, laser treatments, and surgical interventions. While surgical methods like trabeculectomy and minimally invasive glaucoma surgery (MIGS) are very effective in controlling IOP, pharmacological treatment remains first-line treatment for most patients because it is non-invasive and easy to administer[6,8.]

Currently, prostaglandin analogues (PGAs) and β-blockers are the first-line pharmacological treatments for glaucoma. PGAs, such as latanoprost, are favoured for their potent IOP-lowering effects, primarily achieved by increasing uveoscleral outflow[8]. β-blockers, on the other hand, act by reducing the production of aqueous humor[9-12].

Among the newer pharmacological agents marketed for glaucoma management is Ripasudil, a

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Rho kinase inhibitor, which represents a novel mechanism. In contrast, PGAs stimulate uveoscleral outflow, and Ripasudil increases drainage of aqueous humor through the trabecular meshwork that targets the conventional outflow pathway[13-17]. This would make Ripasudil a promising adjunctive therapy for IOP-reducing patients. Another adjunctive agent, used in the majority of cases, includes Dorzolamide, a carbonic anhydrase inhibitor that inhibits the enzyme carbonic anhydrase located in the ciliary processes, thereby reducing aqueous humor production. The introduction of Ripasudil has expanded the range of therapeutic options available for glaucoma management, especially in cases of non-response to traditional treatments. Addressing different pathways in the regulation of aqueous humor dynamics by this drug complements the effects of PGAs and gives a valuable addition to combination drug therapy[18,19]. The safety and efficacy of Ripasudil as an add-on treatment, therefore, continue to be explored in research and have been compared with established agents such asDorzolamide[20].

This study is aimed at determining the comparative safety and efficacy profiles of Ripasudil and Dorzolamide as adjuncts to PGAs in patients with glaucoma and their IOP-lowering potential, tolerability, and overall clinical utility in achieving target IOP levels. The burden of glaucoma on public health is significant, and the increasing need for effective treatment strategies has made it necessary to understand the role of novel agents, such as Ripasudil, in combination therapies to optimise patient outcomes[21-23]. Besides discussing the pharmacological mechanisms underlying their actions, this study aims to contribute to understanding the clinical use of Ripasudil and Dorzolamide in everyday practice. Comparing the efficacy and safety of these drugs will help clinicians select the most suitable adjunctive treatment for patients who require greater IOP control than is achievable with PGA monotherapy. This study contributes to the evolving landscape of glaucoma management by emphasising the importance of innovative therapeutic approaches in reducing the global burden of blindness from this disease.

Materials and Methods

Study design and participants

This is an interventional prospective study conducted at a tertiary eye centre between January and April. The study recruited 120 patients with primary open-angle glaucoma who had an intraocular pressure that remained inadequately controlled despite latanoprost monotherapy at 0.005%. The study had a 10% dropout rate. Control was deemed inadequate when intraocular pressure remained consistently above the range for glaucoma managementccording to the treating ophthalmologist[24]. Ethical clearance was obtained from the Institutional Ethics Committee for the current study from Chitkara University, the Institutional Human Ethical Committee (IHEC) for human research, under approval number EC/NEW/INST/2021/531/55/I. Written informed consent was also obtained from participants before enrolling them in the study.

The inclusion criteria for the study were patients aged 40 to 80 years with POAG who had been on latanoprost monotherapy for at least 3 months before enrolment. Patients with significant ocular or systemic conditions that could influence IOP or drug response, such as uveitis, ocular trauma, advanced diabetes, or uncontrolled hypertension, were excluded from the study. They also excluded patients having a history of hypersensitivity or allergic reaction to Ripasudil or Dorzolamide in order to avoid reactions[24]. These patients were randomly assigned to one of the two following groups; Group A: These patients were administered 0.4% Ripasudil eye drops, and their current regimen of latanoprost was continued, administered twice daily and Group B: Patients in this group received 2% Dorzolamide eye drops twice a day in conjunction with latanoprost.

Randomisation and sample size

Participants were allocated using simple randomisation to ensure unbiased assignment; allocation concealment was ensured by the principal investigator, who stored the randomisation list in a locked file folder, access to which was permitted only after participant enrolment was complete. The sample size was estimated based on the expected effect size and the desired statistical power to achieve precision in estimating group differences. The sample size was calculated to detect a minimum 20% difference in IOP reduction between groups, with 80% power and 5% significance, resulting in a requirement of at least 50 patients per arm. To account for potential dropouts, 60 patients were randomly assigned to each group using computer-generated random numbers with allocation concealment. Group A (n=60): Ripasudil 0.4% twice daily + latanoprost; Group B (n=60): Dorzolamide 2% twice daily + latanoprost.

Preliminary examinations

All patients underwent rigorous baseline ophthalmological examinations by an experienced ophthalmologist before the start of the study protocol. These included the[24,25], Medical and Ocular history: A detailed history of systemic and ocular conditions was recorded, including previous treatments, allergies, and surgeries; Uncorrected and Best-Corrected Visual Acuity: Baseline visual function was assessed by the measurement of uncorrected and best-corrected visual acuity.

Tonometry

IOP was assessed with Goldmann applanation tonometry, which is the gold standard for IOP measurements. Three readings were taken per visit and recorded as a mean value to increase accuracy.

Schirmer's test

Tear production was evaluated to exclude significant dry eye syndrome, which could interfere with drug tolerability or efficacy.

Slit-Lamp Biomicroscopy

The anterior segment was evaluated for corneal clarity, depth of the anterior chamber, and other structural parameters.

Dilated Fundus examination:

The posterior segment, including the optic disc and retina, was examined for evidence of glaucomatous damage or other retinal pathologies.

Study protocol

After the baseline assessment, patients in both groups commenced combination therapy, instilling either Ripasudil or Dorzolamide twice daily in addition to latanoprost. To encourage adherence, each patient was carefully counselled and provided with a diary to record instillation times and any missed doses[26]. IOP was measured at baseline and at each follow-up visit, with readings obtained at three fixed time points daily (9:00 a.m., 1:00 p.m., and 5:00 p.m.). The mean of these three values was used for analysis to minimise the influence of diurnal variation. The primary outcome was the reduction in IOP from baseline, compared between the two groups. Conjunctival hyperaemia, a well-recognised side effect of ripasudil, was assessed at every visit using the CCLRU grading scale (0 = none, 4 = severe)[21,22,27].

To ensure consistency, the same examiner performed all IOP measurements and hyperemia grading throughout the study. Adverse events, including ocular discomfort, blurred vision, or systemic reactions, were recorded and monitored to evaluate tolerability[18].

This robust methodological framework ensured that the effectiveness and safety of Ripasudil and Dorzolamide as adjunctive therapies for treating glaucoma were thoroughly evaluated.

Statistical analysis

Data were analysed using SPSS version 26. Baseline characteristics were summarised descriptively. Within-group changes in IOP were analysed using paired *t*-tests, while between-group comparisons employed independent *t*-tests after verifying the normality of the distributions, which were found to be normally distributed. The frequency and severity of side effects were assessed using chi-square tests. A *P*-value < 0.05 was considered statistically significant[19].

Results

Demographic and clinical characteristics

A total of 120 patients were taken, diagnosed with primary open-angle glaucoma (POAG), who required additional therapy for adequate IOP control beyond latanoprost monotherapy. Patients were randomly assigned to two equal groups: Group A: Ripasudil + Latanoprost (n = 60) and Group B: Dorzolamide + Latanoprost (n = 60)

The demographic characteristics of the participants are summarised in Table 1. For Group A, the mean age was 66 ± 8.2 years (range: 45–78 years), while for Group B, it was 64 ± 9.1 years (range: 42–80 years). The age distribution did not differ significantly between the two groups ($P > 0.05$).

Gender distribution was also comparable, as shown in Table 1. The male-to-female ratio was 1:1 (30 males, 30 females) in group A, while it was approximately 1.1:1 (32 males, 28 females) in Group

Table 1 — Baseline demographic characteristics of patients

Variable	Group A (Ripasudil + Latanoprost, n=60)	Group B (Dorzolamide + Latanoprost, n=60)	*P* value
Age (Mean ± SD, Range)	66 ± 8.2 (45–78)	64 ± 9.1 (42–80)	0.27
Male:Female ratio	30:30	32:28	0.82

B. This close matching in age and gender minimised the risk of demographic bias influencing treatment outcomes.

Baseline IOP values before initiation of adjunctive therapy are detailed in Table 2. The two groups demonstrated similar mean IOP levels at baseline, confirming that the study groups were well matched in terms of disease severity prior to intervention. To enhance accuracy, IOP was measured at three fixed time points daily (9:00 a.m. 1:00 p.m. and 5:00 p.m.), and the mean of these values was used for analysis.

Intraocular pressure reduction

Over the 12-week follow-up period, both groups exhibited a progressive reduction in IOP from baseline; however, the effect was more pronounced in the ripasudil group. At week 1, the mean IOP reduction was –4.8 ± 1.1 mmHg in Group A compared to –3.9 ± 1.0 mmHg in Group B (P = 0.03). By week 4, the reduction reached –6.7 ± 1.5 mmHg in Group A and –5.4 ± 1.4 mmHg in Group B (P = 0.01). This trend continued at week 8 (–7.0 ± 1.6 *vs* –5.8 ± 1.3 mmHg; P = 0.01) and week 12 (–7.2 ± 1.4 *vs* –6.0 ± 1.5 mmHg; P = 0.01), confirming that ripasudil as an adjunct to latanoprost achieved greater IOP control compared to dorzolamide, as shown in Table 3 & Fig. 1.

Conjunctival hyperemia

Conjunctival hyperemia was more frequently observed in the Ripasudil group, though the majority of cases were mild. In Group A, 12 patients (20%) experienced hyperemia: 8 had mild (grade 1), 3 had moderate (grade 2), and 1 had severe (grade 3) hyperemia. In contrast, only 6 patients (10%) in Group B developed hyperemia, of which 5 were mild and 1 moderate, with no severe cases. No patient in either group developed grade 4 hyperemia. The difference between the groups was not statistically significant (P > 0.05) Table 4 & Fig. 2.

Table 2 — Baseline intraocular pressure (IOP, mmHg)

Time of measurement	Group A (Mean ± SD)	Group B (Mean ± SD)	P value
9:00 a.m.	24.3 ± 2.1	24.1 ± 2.3	0.64
1:00 p.m.	23.9 ± 2.0	24.0 ± 2.1	0.88
5:00 p.m.	23.6 ± 1.9	23.8 ± 2.0	0.73
Daily Mean	23.9 ± 2.0	24.0 ± 2.1	0.77

Table 3 — Mean reduction in IOP over 12 weeks

Follow-up week	Group A (Mean ± SD)	Group B (Mean ± SD)	Between-group P value
Week 1	–4.8 ± 1.1	–3.9 ± 1.0	0.03*
Week 4	–6.7 ± 1.5	–5.4 ± 1.4	0.01*
Week 8	–7.0 ± 1.6	–5.8 ± 1.3	0.01*
Week 12	–7.2 ± 1.4	–6.0 ± 1.5	0.01*

[*Statistically significant (P < 0.05)]

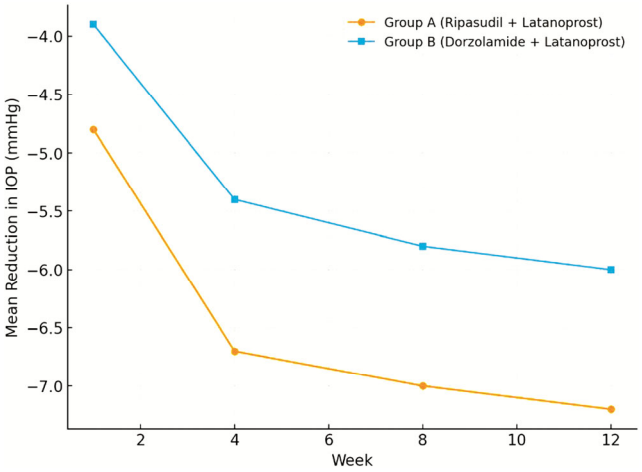

Fig. 1 — Comparative IOP reduction in Group A and Group B. Line graph showing the mean reduction in intraocular pressure (mmHg) at different follow-up time points in Group A (Ripasudil + Latanoprost) and Group B (Dorzolamide + Latanoprost). Both groups demonstrated a progressive reduction in IOP over time, with Group A showing a greater reduction compared with Group B during the follow-up period. Values represent the mean IOP reduction at each visit.

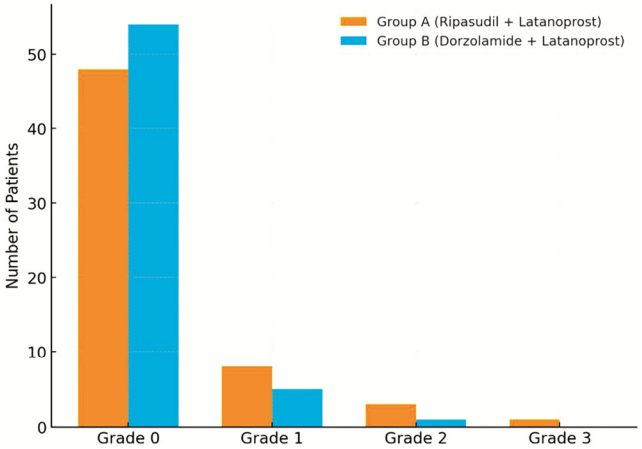

Fig. 2 — Conjunctival Hyperemia Grading. Bar chart illustrating the number of patients in each conjunctival hyperemia grade (Grade 0–3) in Group A (Ripasudil + Latanoprost) and Group B (Dorzolamide + Latanoprost). Most patients in both groups had Grade 0 hyperemia, while higher grades were less frequent.

Table 4 — Conjunctival hyperemia grading (CCLRU scale)

Grade (0-4)	Group A (%)	Group B (%)	P value
0 (None)	48 (80%)	54 (90%)	0.18
1 (Mild)	8 (13.3%)	5 (8.3%)	0.41
2 (Moderate)	3 (5%)	1 (1.7%)	0.62
3-4 (Severe)	1 (1.7%)	0 (0%)	0.31

Adverse events

Other adverse events were uncommon and generally mild in both groups. In Group A, ocular discomfort was reported by 6 patients (10%), blurred vision by 3 patients (5%), and systemic side effects by 1 patient (1.7%). In Group B, ocular discomfort occurred in 4 patients (6.7%), and blurred vision occurred in 2 patients (3.3%), while no systemic adverse effects were reported. The overall incidence of adverse events was 16.7% in Group A and 10% in Group B, but this difference was not statistically significant ($P > 0.05$), Table 5 & Fig. 3.

Discussion

This study highlights that Ripasudil and Dorzolamide are effective add-on treatments in combination with prostaglandin analogues (PGAs) to reduce intraocular pressure (IOP) in patients with glaucoma. Both drugs elicited significant effects on IOP lowering when given in combination with latanoprost, which is one of the most prescribed PGAs[28,29]. Efficacy was consistently better in the Ripasudil group, achieving a reduction in IOP of up to 7–12% greater compared to the Dorzolamide group.

Table 5 — Adverse events reported during the study

Adverse event	Group A (n=60)	Group B (n=60)	P value
Ocular discomfort	6 (10%)	4 (6.7%)	0.52
Blurred vision	3 (5%)	2 (3.3%)	0.65
Systemic side effects	1 (1.7%)	0 (0%)	0.31
Any adverse event	10 (16.7%)	6 (10%)	0.29

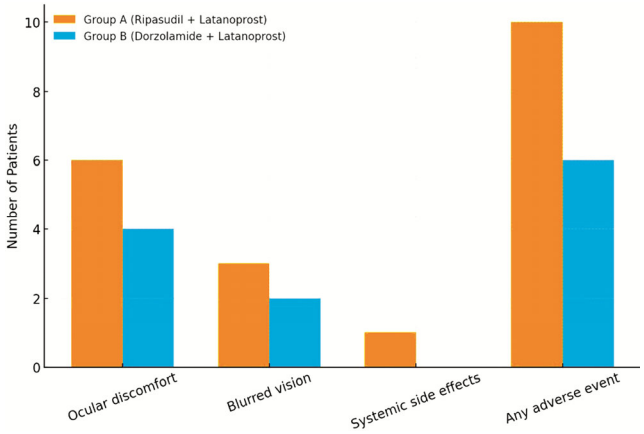

Fig. 3 — Adverse Events Reported During Study. Bar chart showing the frequency of adverse events, including ocular discomfort, blurred vision, systemic side effects, and overall adverse events, in Group A (Ripasudil + Latanoprost) and Group B (Dorzolamide + Latanoprost). Ocular discomfort was the most commonly reported adverse event, while systemic side effects were infrequent in both groups.

This difference reached statistical significance at all follow-up visits, indicating that Ripasudil provided superior adjunctive IOP-lowering efficacy when combined with latanoprost.

Ripasudil, with its innovative action of aqueous humor outflow through the trabecular meshwork, synergizes well with Latanoprost, which enhances outflow in the uveoscleral pathway. As such, this complementary mechanism makes Ripasudil an extremely beneficial option for patients who require additional IOP lowering beyond what PGAs can provide. In addition, targeting distinct pathways within aqueous humor dynamics has been a strategic advantage in the management of refractory cases of glaucoma30-33.

While highly effective, the most commonly reported side effect associated with Ripasudil use was conjunctival hyperemia, observed in 20% of patients, most cases being mild (Grade 1–2) and transient. Moderate hyperemia occurred in 18% of cases, and severe hyperemia in 9%. Importantly, in all cases, the hyperemia resolved spontaneously within two hours of instillation, indicating that it did not interfere with treatment compliance34-36. These patients also tolerated hyperemia better when given prior notice; thus, there is a significant role for patient education in increasing compliance with the therapy. In contrast, no significant conjunctival hyperemia was detected, but a marginally reduced IOP-reducing response of Dorzolamide was noted with respect to Ripasudil37-39. However, its carbonic anhydrase inhibition mode of action, which reduces the production of aqueous humour, is certainly distinct from the outflow enhancement attributed to Ripasudil action[40]. This suggests that the best therapy should be tailored to the individual patient's tolerability profile.

Limitations and future directions

While the study enlightens us on the comparative efficacy and safety of Ripasudil over Dorzolamide, this study has particular limitations. The study included only 120 participants. Their generalizability is limited based on this sample. A larger study sample size means greater statistical power to detect larger differences between the two groups and more robust conclusions for the study.

Absence of stratification based on disease severity, baseline IOP, or other patient-specific factors limits the ability to determine whether certain subgroups benefit more from one therapy over the other. For example, patients with advanced glaucoma or higher

baseline IOP may respond differently to these treatments. Six-week follow-up provides insight into the short-term efficacy and safety but fails to provide an appreciation of the longer-term effects, including continued IOP control and the risk for cumulative side effects. Although conjunctival hyperaemia was monitored, other potential safety side effects, including corneal effects or systemic effects, were not evaluated in this study.

Future research should tackle these limitations with larger, multicenter studies with longer follow-up periods. Subgroup analyses stratified by disease severity, baseline IOP, and prior treatment history would provide a more nuanced understanding of these drugs' efficacy and safety profiles. Patient-reported outcomes, including quality of life and treatment satisfaction, should be integrated into future studies in order to understand the holistic impact of these therapies.

Conclusion

Overall, the study demonstrates that both Ripasudil and Dorzolamide, when used as adjuncts to prostaglandin analogues, significantly reduce intraocular pressure in glaucoma patients. Ripasudil showed a slightly greater IOP-lowering effect, while associated conjunctival hyperaemia was transient and did not affect adherence. These findings support the adjunctive use of both agents, with Ripasudil offering a modest efficacy advantage.

Conflict of interest

The authors declare that they have no conflict of interest.

Reference

1 Martin Chibueze L. Glaucoma in Nigeria-factors influencing late presentation of the disease. 2014.

2 Nuzzi R, Marolo P & Nuzzi A. The Hub-and-Spoke Management of Glaucoma. *Front Neurosci*. 14 (2020) 180.

3 Trivli A, Koliarakis I, Terzidou C, Goulielmos G, Siganos C, Spandidos D, Dalianis G & Detorakis ET. Normal-tension glaucoma: Pathogenesis and genetics (Review). *Exp Ther Med*. 17 (2019) 563.

4 Prum BE, Lim MC, Mansberger SL, Stein JD, Moroi SE, Gedde SJ, Herndon LW Jr, Rosenberg LF & Williams RD. Primary Open-Angle Glaucoma Suspect. *Ophthalmology*. 123 (2016) 112.

5 Lee JWY, Chan PP, Zhang XJ, Chen LJ & Jonas JB. Latest developments in normal-pressure glaucoma: Diagnosis, epidemiology, genetics, etiology, causes and mechanisms to management. *Asia Pac J Ophthalmol*, 8 (2019) 457.

6 Ciobanu AM, Dionisie V, Neagu C, Bolog OM, Riga S & Popa-Velea O. Psychopharmacological treatment, intraocular pressure and the risk of glaucoma: A review of literature. *J Clin Med*. 10 (2021) 294.

7 Sharfuddin Ahmed M, Ullah AY, Barman N, Ratan ZA, Mostafa S, Khaleque A, Kabir S, Khan MH & Haque MA. Risk factors associated with elevated intraocular pressure: A population-based study in a rural community of Bangladesh. *BMJ Open Ophthalmol*. 8 (2023) e001386.

8 Gillmann K. Towards Personalised Glaucoma Management Identification of Specific Factors Influencing Glaucoma Treatment Outcomes. 2022.

9 Virani S & Rewri P. An Update on Pharmacotherapy of Glaucoma. 2023.

10 Wang T, Cao L, Jiang Q & Zhang T. Topical Medication Therapy for Glaucoma and Ocular Hypertension. *Front Pharmacol*. 12 (2021) 749858.

11 Kandarakis SA, Togka KA, Doumazos L, Mylona I, Katsimpris A, Petrou P & Kymionis G. The Multifarious Effects of Various Glaucoma Pharmacotherapy on Corneal Endothelium: A Narrative Review. *Ophthalmol Ther*. 12 (2023) 1457.

12 Khaw PT, Bouremel Y, Brocchini S & Henein C. The control of conjunctival fibrosis as a paradigm for the prevention of ocular fibrosis-related blindness. “Fibrosis has many friends”. *Eye*, 34 (2020) 2163.

13 Kusuhara S & Nakamura M. Ripasudil hydrochloride hydrate in the treatment of glaucoma: Safety, efficacy, and patient selection. *Clinical Ophthalmology*. 14 (2020) 1229.

14 Gopalakrishna M & Kavitha S. Rho-kinase inhibitors in ophthalmology. *TNOA J. of Ophth Scie Res.*59 (2021) 56.

15 Pagano L, Lee JW, Posarelli M, Giannaccare G, Kaye S & Borgia A. ROCK Inhibitors in Corneal Diseases and Glaucoma—A Comprehensive Review of These Emerging Drugs. *J Clin Med*. 12 (2023) 6736.

16 Yoshida T, Yoshimoto S, Nomura T, Ito T, Ohno M, Yasuda S, Shiotani Y, Ohno-Matsui K. Intraocular pressure-lowering effects of ripasudil on open-angle glaucoma in eyes with high myopia and pathological myopia. *Sci Rep.*13 (2023) 22888.

17 Wang J, Wang H & Dang Y. Rho-Kinase Inhibitors as Emerging Targets for Glaucoma Therapy. *Ophthalmol Ther.* 12 (2023) 2943.

18 Minami Y, Song Y seok, Ishibazawa A, Omae T, Ro-mase T, ishiko S & Yoshida A. Effect of ripasudil on diabetic macular edema. *Sci Rep*. 9 (2019) 3703 .

19 Naik M, Kapur M, Gupta V, Sethi H & Srivastava K. Ripasudil endgame: Role of rho-kinase inhibitor as a last-ditch-stand towards maximally tolerated medical therapy to a patient of advanced glaucoma. *Clin Ophthalmol*. 15 (2021) 2683.

20 Tanihara H, Inoue T, Yamamoto T, Kuwayama Y, Abe H, Suganami H & Araie M. Intra-ocular pressure-lowering effects of a Rho kinase inhibitor, ripasudil (K-115), over 24 hours in primary open-angle glaucoma and ocular hypertension: A randomized, open-label, crossover study. *Acta Ophthalmol*. 93 (2015) Jun e254.

21 Wang T, Cao L, Jiang Q & Zhang T. Topical Medication Therapy for Glaucoma and Ocular Hypertension. *Front Pharmacol*. 12 (2021) 749858.

22 Jayanetti V, Sandhu S & Lusthaus JA. The latest drugs in development that reduce intraocular pressure in ocular hypertension and glaucoma. *J Exp Pharmacol*. 12 (2020) 539.

23 Aref AA, Geyman LS, Zakieh AR & Alotaibi HM. Netarsudil and latanoprost ophthalmic solution for the reduction of intraocular pressure in open-angle glaucoma or ocular hypertension. *Expert Rev Clin Pharmacol*. 12 (2019) 1073.

24 Razali N, Shafiq Hassan MD, Abu Bakar AS & Agarwal R. Medical Management of Open-Angle Glaucoma: Focus on Mechanisms of Action and Adverse Drug Reactions. *J. basic clin. health sci,* 6 (2021) 4.

25 Jayanetti V, Sandhu S & Lusthaus JA. The latest drugs in development that reduce intraocular pressure in ocular hypertension and glaucoma. *J Exp Pharmacol. 12* (2020) 539.

26 Al-Namaeh M. Pharmaceutical treatment of primary open angle glaucoma. *Med. Hypoth. Discov. Innov. Opto.* 2 (2021) 8.

27 Sinha S, Lee D, Kolomeyer NN, Myers JS & Razeghinejad R. Fixed combination netarsudil-latanoprost for the treatment of glaucoma and ocular hypertension. *Expert Opin Pharmacother*. 21 (2020) 39.

28 Wang T, Cao L, Jiang Q & Zhang T. Topical Medication Therapy for Glaucoma and Ocular Hypertension. *Front Pharmacol*. 12 (2021) 749858.

29 Iannucci V, Manni P, Mecarelli G, Giammaria S, Giovannetti F, Lambiase A & Alice Bruscolini. Childhood Uveitic Glaucoma: Complex Management in a Fragile Population. *App Scie*. 13 (2023) 2205.

30 Kaneko Y, Ohta M, Inoue T, Mizuno K, Isobe T, Tanabe S & Tanihara H. Effects of K-115 (Ripasudil), a novel ROCK inhibitor, on trabecular meshwork and Schlemms canal endothelial cells. *Sci Rep*. 6 (2016) 19640.

31 Al-Humimat G, Marashdeh I, Daradkeh D & Kooner K. Investigational rho kinase inhibitors for the treatment of glaucoma. *J Exp Pharmaco,*13 (2021) 197.

32 Wang C, Dang Y, Waxman S, Hong Y, Shah P, Loewen RT, Xia X & Loewen NA. Ripasudil in a model of pigmentary glaucoma. *Transl Vis Sci Technol*. 9 (2020) 1.

33 Goda E, Hirooka K, Mori K & Kiuchi Y. Intraocular pressure-lowering effects of Ripasudil: A potential outcome marker for Trabeculotomy. *BMC Ophthalmol*. 19 (2019) 243.

34 Araie M, Sugiyama K, Aso K, Kanemoto K, Iwata R, Hollander DA, Senchyna M & Kopczynski CC. Phase 3 Clinical Trial Comparing the Safety and Efficacy of Netarsudil to Ripasudil in Patients with Primary Open-Angle Glaucoma or Ocular Hypertension: Japan Rho Kinase Elevated Intraocular Pressure Treatment Trial (J-ROCKET). *Adv Ther*. 40 (2023) 4639.

35 Tanihara H, Kakuda T, Sano T, Kanno T & Kurihara Y. Long-Term Intraocular Pressure-Lowering Effects and Adverse Events of Ripasudil in Patients with Glaucoma or Ocular Hypertension over 24 Months. *Adv Ther*. 39 (2022)1659.

36 Terao E, Nakakura S, Fujisawa Y, Fujio Y, Matsuya K, Kobayashi Y, Tabuchi H, Yoneda T, Fukushima A & Kiuchi Y. Time Course of Conjunctival Hyperaemia Induced by a Rho-kinase Inhibitor Anti-glaucoma Eye Drop: Ripasudil 0.4%. *Curr Eye Res*. 42 (2017) 738.

37 Lee NY, Park HYL & Park CK. Comparison of the effects of dorzolamide/timolol fixed combination versus latanoprost on intraocular pressure and ocular perfusion pressure in patients with normal-tension glaucoma: A randomized, crossover clinical trial. *PLoS One.* 11 (2016) e0146680.

38 Lin WC, Hsieh JW, Tsai S & Lan YW. Latanoprost-Associated cystoid macular edema in a patient with phakic eyes. Taiwan J Ophthalmol. 13 (2023) 242.

39 Konstas AG, Schmetterer L, Katsanos A, Hutnik CML, Holló G, Quaranta L, Teus , Pfeiffer N & Katz LJ. Dorzolamide/Timolol Fixed Combination: Learning from the Past and Looking Toward the Future. *Adv Ther*. 38 (2021) 24.

40 Occhipinti R & Boron WF. Role of carbonic anhydrases and inhibitors in acid–base physiology: Insights from mathematical modeling. *Int J Mol Sci*. 20 (2019) 3841.