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REAL-WORLD STUDY

Real-world use of a hydrophilic curcumin-based oral formulation in the management of macular oedema: a collection of clinical experiences

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Abstract

This is a collection of clinical experiences exploring the real-world effectiveness of a hydrophilic curcumin-based oral formulation (CHC, Diabec®) in the management of macular oedema across diverse retinal conditions, including diabetic macular oedema, central serous chorioretinopathy, branch retinal vein occlusion and Irvine–Gass syndrome. Eight cases reported significant improvements in best-corrected visual acuity and central macular thickness, with complete resolution of oedema in some instances. CHC was well tolerated, with no adverse effects reported. These findings suggest that CHC is a safe and effective adjunct or standalone therapy for chronic or refractory macular oedema, enhancing anatomical and functional outcomes in real-world settings.

Keywords: central serous chorioretinopathy, curcumin-based therapy, diabetic macular oedema, hydrophilic carrier curcumin, macular oedema.

Citation

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Introduction

Macular oedema (MO) is a major cause of visual impairment and is associated with several retinal diseases, including diabetic retinopathy (DR), retinal vein occlusion (RVO) and uveitis.[1–3] MO results from the disruption of the blood–retinal barrier, leading to intra-retinal and/or sub-retinal fluid accumulation, ultimately causing functional and anatomical retinal deterioration.[1] Despite advances in treatment strategies, including anti-vascular endothelial growth factor (VEGF) agents, corticosteroids and laser therapy, controlling MO, especially in chronic or refractory cases, remains a challenge.[4]

Curcumin, a polyphenolic compound derived from *Curcuma longa*, has garnered attention for its anti-inflammatory, antioxidant and antiangiogenic properties.[5] Curcumin exerts its effects through the modulation of multiple molecular pathways, including the inhibition of pro-inflammatory cytokines (TNF, IL-6, IL-1β) and VEGF, which are crucial in the pathogenesis of MO.[6] Indeed, these mediators can increase vascular permeability and disrupt the blood–retinal barrier. Furthermore, curcumin has been shown to protect retinal cells from oxidative stress and prevent neurodegeneration, which are common in chronic retinal diseases, such as DR and central serous chorioretinopathy (CSC).[7]

Despite these beneficial properties, the therapeutic use of curcumin in clinical practice has been limited due to its low bioavailability, rapid metabolism and systemic clearance.[8] To overcome these limitations, the combination

of a curcumin formulation (CurcuWIN® Dry Powder 20%) with a polyvinylpyrrolidone hydrophilic carrier (CHC; Diabec®, Alfa Intes, Naples, Italy) was compared to other formulations and showed enhanced bioavailability in the blood and retina after a single oral administration.[9–11] This improved bioavailability allows CHC to reach therapeutic concentrations in the retina, making it an effective adjuvant in the treatment of MO. Accordingly, recent clinical trials reported significant improvements in both visual acuity (VA) and retinal morphology with CHC treatment when combined with standard treatments, such as corticosteroids. In particular, studies on diabetic MO (DMO), non-infectious uveitic MO and MO of various uncommon aetiologies (including CSC and post-traumatic oedema) have highlighted the therapeutic potential of CHC in reducing the central retinal thickness and preventing recurrence as well as its good safety profile.[12–14]

Although clinical trials reported the efficacy of CHC as an adjunctive treatment for MO in various retinal pathologies, real-world clinical practice experiences on this topic are still scant. This paper aims to fill the literature gap on real-world experiences by presenting a series of clinical cases that describe the use of CHC in daily clinical practice, contributing to a broader understanding of its effectiveness and safety for the management of MO in real-world settings.

Patients and methods

The authors retrospectively reviewed and described clinical cases of patients with MO secondary to various retinal diseases treated with CHC either as monotherapy or in combination with standard therapies. Inclusion criteria were age ≥18 years and an indication of the treatment with CHC based on the physician's routine clinical practice. Ocular complications are reported on a patient-by-patient basis. Due to the retrospective description of this case series, treatment regimens and patient education were not standardized nor was the follow-up schedule. The study was conducted in accordance with the ethical principles of the revised version of the Declaration of Helsinki (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). Best-corrected VA (BCVA) was measured and recorded in Snellen decimal. All patients provided written informed consent to the treatment and publication of clinical data and any accompanying images. CHC was administered according to doses and modalities defined in the summary of product characteristics (one tablet twice daily, for at least 1 month, for acute inflammatory retinal conditions; one or two tablets daily in case of chronic retinal diseases).

Ethics approval: The retrospective review of patient data was notified to the Ethics Committee of the participating centre when required.

Clinical cases

The authors retrospectively selected and reported clinical experiences related to eight patients treated with CHC. The main demographic and clinical characteristics of patients are presented in Table 1; a detailed description of each case is reported in the following paragraphs.

CHC for the management of Irvine–Gass syndrome

A 75-year-old man with a medical history of systemic hypertension and glaucoma, managed with prostaglandin analogue eye drops, presented in February 2023, with decreased vision in the right eye (RE). The patient had undergone cataract surgery on the RE 1 month prior and reported a significant decline in vision since the procedure. Post-surgery, he was treated with a topical combined antibiotic-steroid drop (chloramphenicol-betamethasone 1 mg/2.5 mg) five times daily for 15 days, along with a topical non-steroidal anti-inflammatory drop (indomethacin) three times daily for 30 days. At the initial visit, his BCVA in the RE was 0.7, and Spectralis spectral-domain optical coherence tomography (OCT; Heidelberg Engineering, Inc., Heidelberg, Germany) revealed early signs of cystoid MO, including a central retinal thickness (CRT) of 562 µm with intra-retinal fluid and a slight neuroepithelial detachment (Figure 1A). Intraocular pressure (IOP; Goldman Haag Streit applanation tonometer) was 17 mmHg. Based on these findings, the patient was diagnosed with Irvine–Gass syndrome (post-cataract surgery MO), and monotherapy with CHC was prescribed (one tablet twice daily) for 1 month.

At the follow-up visit in March 2023, the patient's BCVA in the RE had improved to 0.9. OCT imaging showed complete resolution of the neuroepithelial detachment and a significant reduction in intra-retinal fluid. CRT thickening persisted (388 µm) but cystoid MO was considerably reduced (Figure 1B). IOP remained stable at 16 mmHg. CHC treatment was continued for 2 additional months with the same dosage (1 tablet twice daily).

By the next follow-up visit in May 2023, the patient's BCVA further improved to 0.9–1.0, and OCT confirmed the complete resolution of cystis. The patient's IOP remained stable at 16 mmHg, and treatment with CHC was discontinued.

At the final follow-up 1 year later, in May 2024, the patient's BCVA remained stable at 1.0. OCT confirmed the complete reabsorption of cystis, whilst CRT was slightly reduced to 381 µm (Figure 1C). No additional treatment was prescribed. The patient was advised to undergo annual follow-up examinations.

This case is notable due to the development of post-surgical MO (Irvine–Gass syndrome) in a patient with concurrent glaucoma treated with prostaglandin analogues and mild inner limiting membrane thickening. The combination of these factors may have contributed to the development of cystoid MO. CHC treatment favoured the reabsorption of cystoid MO and full visual recovery, underscoring its role in managing post-operative MO under these conditions.

CHC for the management of diabetic MO

Case 1

A 56-year-old woman with a history of type 2 diabetes, under systemic therapy with metformin (1000 mg twice daily), presented with bilateral visual decline during an ophthalmic evaluation in November 2023. Her systemic history included hypertension but no other significant systemic conditions were reported. Her ophthalmic history revealed moderate DR associated with MO. In March 2023, the patient had undergone focal laser photocoagulation in both eyes for the management of DR. Subsequently, in September 2023, macular grid photocoagulation was performed to address the MO; however, this intervention did not yield significant improvement in terms of intra-retinal fluid reduction. At presentation, the BCVA was 0.5 decimal Snellen in the RE and 0.7 decimal Snellen in the left eye (LE), with no further improvement with optical correction. Ophthalmic examination revealed cortical cataracts in both eyes, contributing to visual impairment. OCT, performed using the TOPCON device (Topcon Corporation, Tokyo, Japan), confirmed the presence of DMO, with cystoid oedema in the RE (central macular thickness (CMT): 366 µm) and diffuse oedema in the marginal region of the LE (CMT: 149 µm) (Figure 2A, B). IOP (integrated blow tonometer in the Tonoref III autorefractometer; Nidek Co., Ltd, Gamagori, Japan) was recorded at 14 mmHg bilaterally. No other significant findings were noted in the anterior segment. The patient was initiated on CHC tablets (one tablet twice daily) as an adjunct to her ongoing systemic therapy, with no additional ophthalmic interventions prescribed at that time. At the first follow-up in April 2024, BCVA showed a slight improvement to 0.6 Snellen in the RE and 0.8 Snellen in the LE, though further correction did not enhance VA. OCT imaging demonstrated a reduction in cystoid oedema in the RE (CMT: 350 µm) and an improvement in intra-retinal fluid accumulation in the marginal region of the LE (CMT: 146 µm). IOP remained stable at 16 mmHg bilaterally. CHC treatment was maintained at the same dosage, with no additional therapeutic modifications introduced. At the second follow-up in June 2024, further improvements were documented. BCVA increased to 0.7 Snellen in the RE and remained stable at 0.8 Snellen in the LE. OCT scans, consistently performed with the TOPCON device, confirmed sustained reabsorption of cystoid oedema in the RE (CMT: 321 µm) and a further reduction in intra-retinal fluid in the marginal region of LE (CMT: 142 µm) (Figure 2C, D). IOP remained stable, with values of 14 mmHg in the RE and 16 mmHg in the LE. CHC therapy was well tolerated, with no reported adverse effects, and was continued. The patient's systemic therapy for diabetes and hypertension remained unchanged. A subsequent follow-up was recommended in 2 months to monitor for potential complications such as possible recurrence of MO or progression of DR, which are not uncommon in patients with persistent retinal fluid or poor metabolic control.

Case 2

A 64-year-old woman with a medical history of type 2 diabetes mellitus and hypertension presented in November 2022 with a primary complaint of reduced vision in her RE. On initial examination, BCVA in the RE was 0.6. OCT (Topcon Corporation, Tokyo, Japan) revealed diabetic MO with a retinal thickness of 384 µm, hard exudates and early cystoid cavities, indicating the presence of moderate DR (Figure 3A). The overall retinal profile was altered, and retinal thickening was observed. IOP was measured using a Goldmann applanation tonometer and was recorded at 16 mmHg. Blood work indicated poor metabolic control, with elevated fasting glucose levels and an HbA1c of 81 mmol/mol.

The patient was prescribed CHC, starting with a regimen of 1 tablet twice daily for 1 month, followed by one tablet daily for 3 additional months as monotherapy. The patient declined the recommended intravitreal anti-VEGF injections, opting to manage her condition with metabolic control and CHC therapy.

At the follow-up visit in March 2023, after 4 months of CHC treatment, the patient's OCT showed a significant reduction in MO, with CMT reduced to 342 µm (Figure 3B). Her BCVA slightly improved to 0.6–0.7 in the RE, and IOP was stable at 15.5 mmHg. The patient was advised to continue CHC therapy (one tablet daily) and scheduled for another follow-up visit in 6 months.

The combination of improved glycaemic control and CHC therapy allowed the patient to avoid intravitreal anti-VEGF injections whilst achieving a reduction in MO and stabilization of visual function. Further follow-up is necessary to monitor for potential progression or recurrence of MO.

CHC for the management of serous detachment of the neuroepithelium in the macular region

A 65-year-old man with a known history of systemic hypertension, dyslipidaemia and obesity presented with a

Table 1. Patient demographic and clinical characteristics

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age (years)	75	56	74	65	57	53	50	54
Sex	Male	Female	Female	Male	Male	Male	Female	Female
Systemic conditions	Glaucoma, hypertension	Hypertension, type 2 diabetes mellitus	Hypertension, type 2 diabetes mellitus	Hypertension, obesity, dyslipidaemia	Hypertension, dyslipidaemia	None	None	None
Ocular diagnosis	Irvine–Gass (post-surgical macular oedema)	Diabetic macular oedema	Diabetic macular oedema	Serous detachment of the macular neuroepithelium	Cystoid macular oedema secondary to branch retinal vein occlusion	Chronic* CSC	Chronic* CSC	Chronic* CSC
Initial visual acuity								
• RE	7/10	5/10	6/10	4/10	10/10	2/10	5/10	10/10
• LE	–	7/10	–	10/10	1/10	7/10	1/10	7/10
Initial OCT findings								
• RE	Cystoid macular oedema, ILM thickening	Cystoid oedema	Cystoid macular oedema (384 µm)	Neuroepithelial detachment	Normal	Normal	Retinal pigment epithelium detachment with neuroepithelial detachment	Normal
• LE	–	Reduced central macular thickness and mild but diffuse intra-retinal oedema in the marginal region of the retina	–	Normal	Cystoid macular oedema	CSC with fluid leakage	Myopic fundus	CSC with subretinal fluid
Intraocular pressure								
• RE	17 mmHg	14 mmHg	16 mmHg	18 mmHg	17 mmHg	12 mmHg	16 mmHg	16 mmHg
• LE	–	14 mmHg	–	18 mmHg	16 mmHg	12 mmHg	16 mmHg	13 mmHg
CHC dosage	1 tablet 2×/day	1 tablet 2×/day	1 tablet day after initial 2×/day for 1 month	1 tablet 2×/day	1 tablet 2×/day	1 tablet 2×/day for 30 days, 1 tablet daily for an additional 30 days	1 tablet 2×/day	1 tablet day after initial 2×/day for 1 month

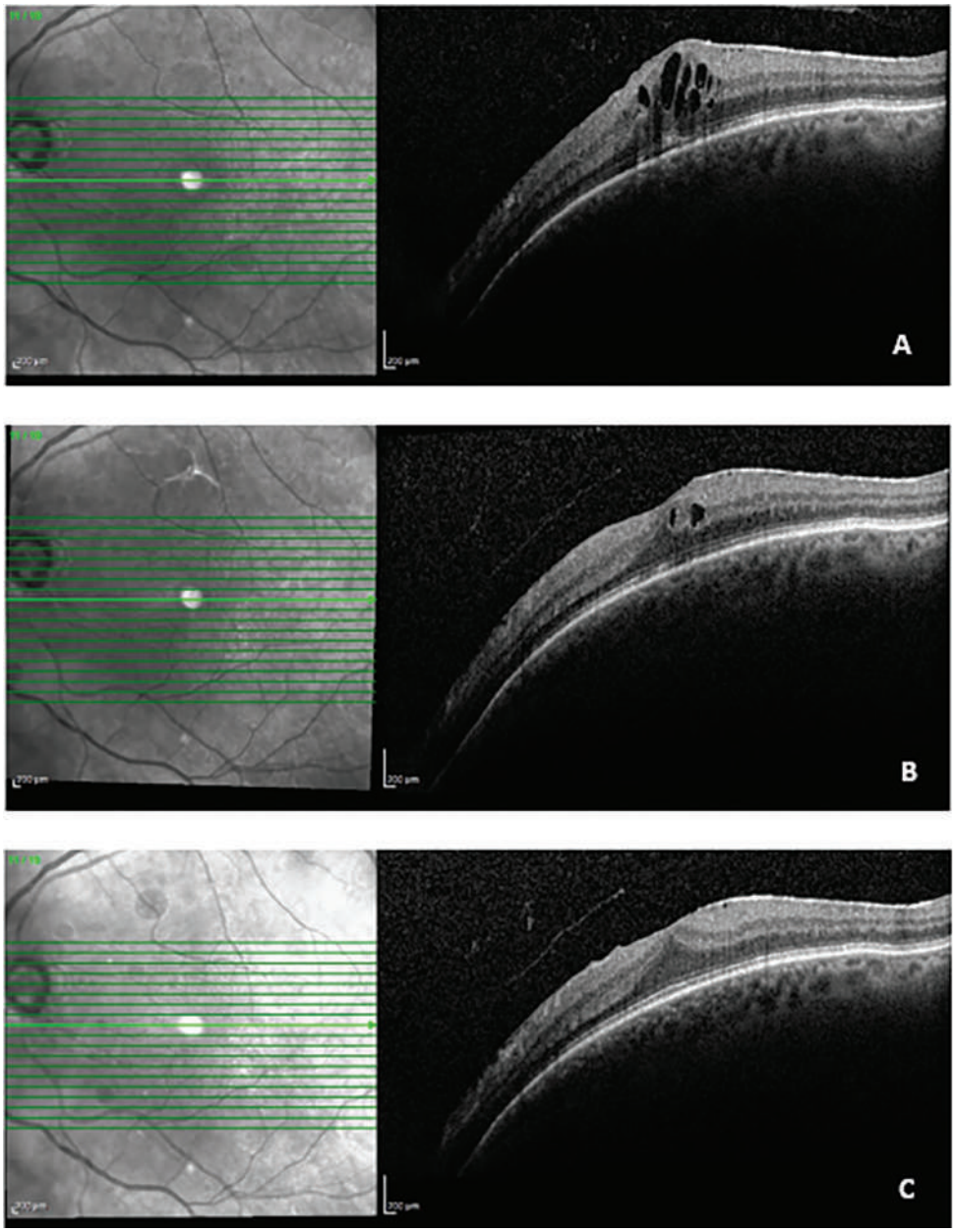
(*Continued*)

Table 1. (Continued)

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Additional therapy	None	None	None	None	Systemic therapy for hypertension and dyslipidaemia, no additional ocular treatments	None	Micro-pulsed laser in RE	None
Previous interventions before CHC initiation	• Cataract surgery on RE (1 month prior) • Topical antibiotic-steroid (chloramphenicol-betamethasone) • Topical non-steroidal anti-inflammatory drug (indomethacin)	• Focal laser photocoagulation in both eyes (8 months prior) • Macular grid photocoagulation (2 months prior)	–	–	Systemic therapy for hypertension and dyslipidaemia	Eplenerone systemic therapy	–	Bromfenac eye drops
Follow-up duration (months)	12	8	4	2	4	15	12	3
Final visual acuity (Snellen)								
• RE	10/10	7/10	6–7/10	8/10	10/10	2/10 (stable)	5/10 (stable)	10/10 (stable)
• LE	–	8/10	–	10/10	5/10	7/10 (improved)	1/10 (stable)	10/10 (improved)
Final OCT findings								
• RE	Reabsorbed cystoid oedema	Resolved cystoid oedema	Reduced oedema (342 µm)	Reduced fluid	Stable	Stable	Slight reduction of fluid	Stable
• LE	–	Resolved diffuse oedema	–	–	Reduced macular oedema	Reduced fluid	Complete resolution of oedema	Reduced sub-retinal fluid

*Intended as CSC persistent for more than 3 months. CHC, hydrophilic curcumin-based oral formulation; CSC, central serous chorioretinopathy; ILM, inner limiting membrane; LE, left eye; OCT, optical coherence tomography; RE, right eye.

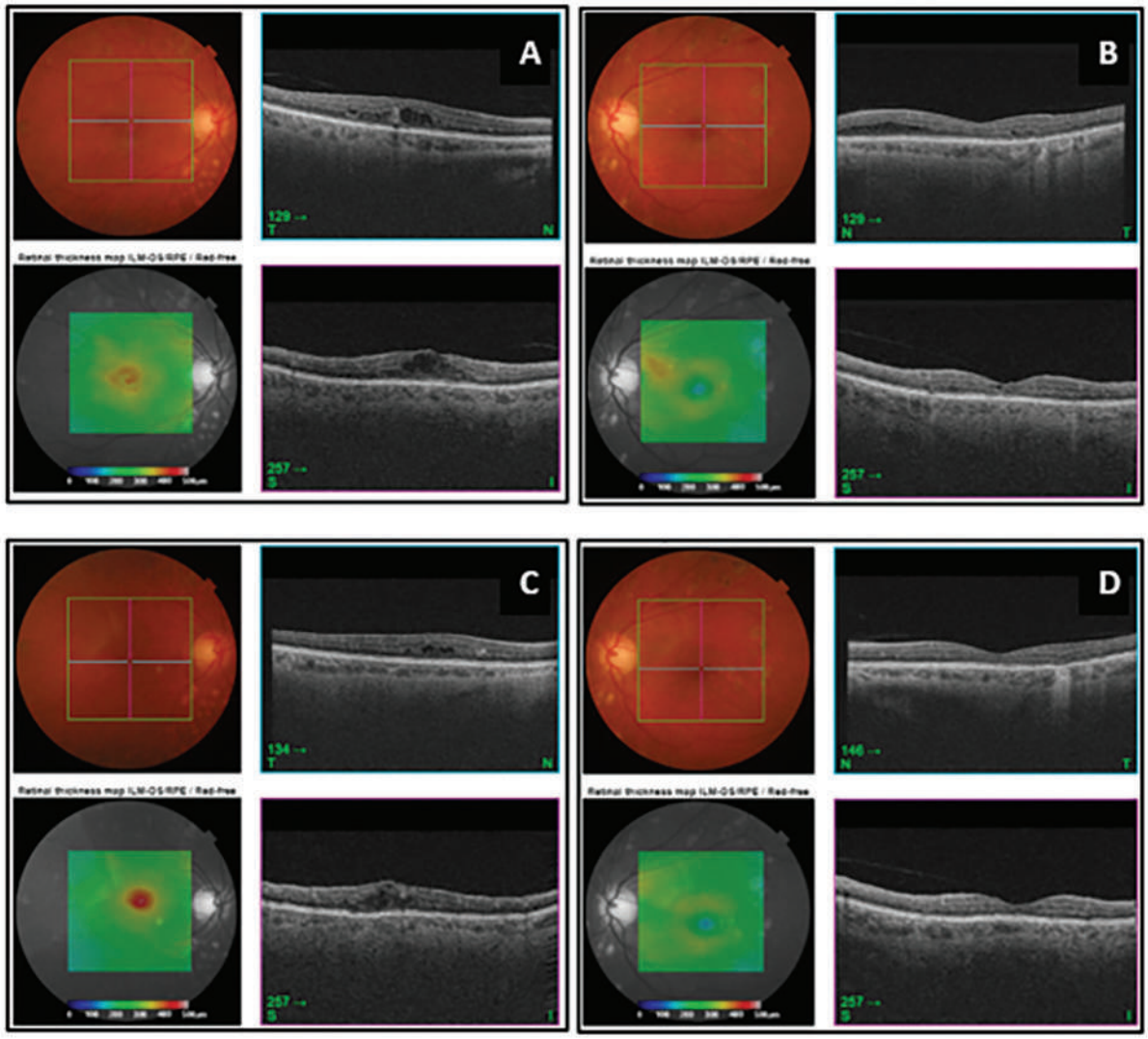
Figure 1. Optical coherence tomography examination in Irvine–Gass syndrome.



A. At presentation, early signs of cystoid macular oedema (MO), including intra-retinal fluid. **B.** MO considerably reduced after 3 months of CHC therapy. **C.** Complete reabsorption of cystoid MO after 1 year.

primary complaint of reduced vision in the RE in March 2024. His medical history was notable for bilateral perifoveal drusen and a type 2 myopic glaucomatous optic disc in both eyes. At initial examination, his BCVA was 0.4 in the RE and 1.0 in the LE, with no potential for improvement with refractive correction. Ophthalmic examination revealed perifoveal drusen and neuroepithelial detachment in the macular region of the RE, with a CMT of 194 µm, whilst the LE exhibited no significant pathological alterations other than perifoveal drusen and a type 2 myopic glaucomatous optic disc. IOP (integrated blow tonometer in the Tonoref III autorefractometer; Nidek Co., Ltd, Gamagori, Japan) was 18 mmHg in both eyes, within normal limits. OCT (Topcon Corporation, Tokyo, Japan) and angiographic OCT confirmed the presence of neuroepithelial detachment in the macular region of the RE, leading to a diagnosis of serous detachment of the neuroepithelium in the macular area, considering also a differential diagnosis with Vogt–Koyanagi–Harada syndrome due to the absence of systemic symptoms, bilateral ocular involvement, chronic uveitis, and dermatological and auditory involvement that characterize this condition (Figure 4A). The presence

Figure 2. Optical coherence tomography examination in diabetic macular oedema, case 1.



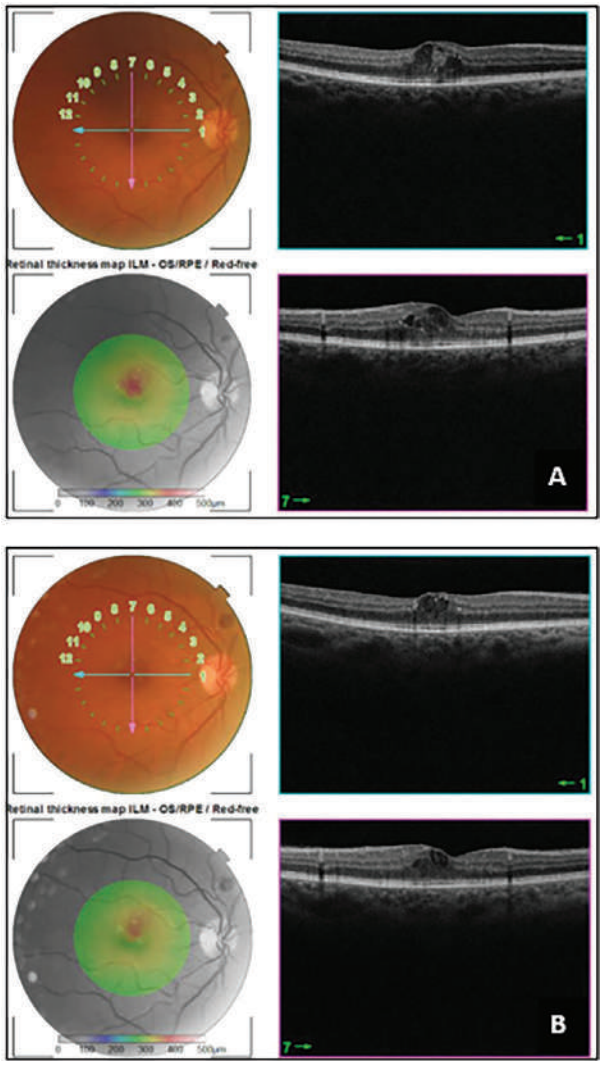
A. Right eye at presentation (November 2023): cystoid macular oedema with central macular thickness (CMT) of 366 µm and best-corrected visual acuity (BCVA) of 0.5 Snellen; **B.** Left eye at presentation (November 2023): diffuse intra-retinal oedema in the marginal region with CMT of 149 µm and BCVA of 0.7 Snellen; **C.** Right eye after 7 months of CHC therapy (June 2024): sustained resolution of cystoid macular oedema with CMT of 321 µm and BCVA of 0.7 Snellen; **D.** Left eye after 7 months of CHC therapy (June 2024): improvement in the reduction of intra-retinal fluid in the marginal region with CMT of 142 µm and BCVA of 0.8 Snellen.

of a neovascular membrane was ruled out through both angiographic OCT and fluorescein angiography (FAG). The patient was treated with CHC (one tablet twice daily) without the addition of further ocular therapies. Systemic treatment for hypertension, dyslipidaemia and obesity was maintained unchanged. At the first follow-up in May 2024, the patient reported significant visual improvement, with BCVA increasing to 0.8 in the RE whilst remaining stable at 1.0 in the LE. OCT imaging demonstrated a complete resolution of the sub-retinal fluid in the macular region, with a reduction in CMT to 174 µm (Figure 4B). Perifoveal drusen remained stable in both eyes, with no evidence of new neuroepithelial detachments. IOP was reduced to 16 mmHg in both eyes. The patient continued taking CHC as prescribed, without reporting adverse effects, and systemic therapy remained unchanged. A second follow-up was scheduled in 2 months to monitor for potential complications or recurrence of macular detachment. This case highlights the potential efficacy of CHC in resolving neuroepithelial detachment, with marked anatomical improvement and partial restoration of visual function.

CHC for the management of MO secondary to a branch RVO

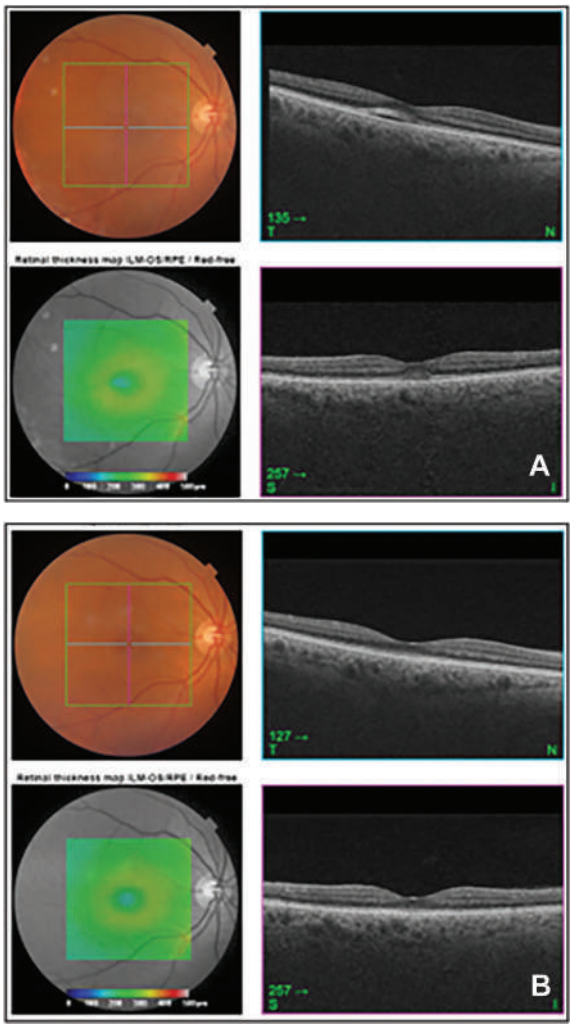
A 57-year-old man with a medical history significant for systemic hypertension and dyslipidaemia presented

Figure 3. Optical coherence tomography examination in diabetic macular oedema, case 2.



A. Diabetic macular oedema at presentation, with a retinal thickness of 384 µm, hard exudates and early cystoid cavities. **B.** After 4 months of CHC treatment, there was a reduction in macular oedema, with central macular thickness reduced to 342 µm.

Figure 4. Optical coherence tomography examination in serous detachment of the neuroepithelium in the macular region.

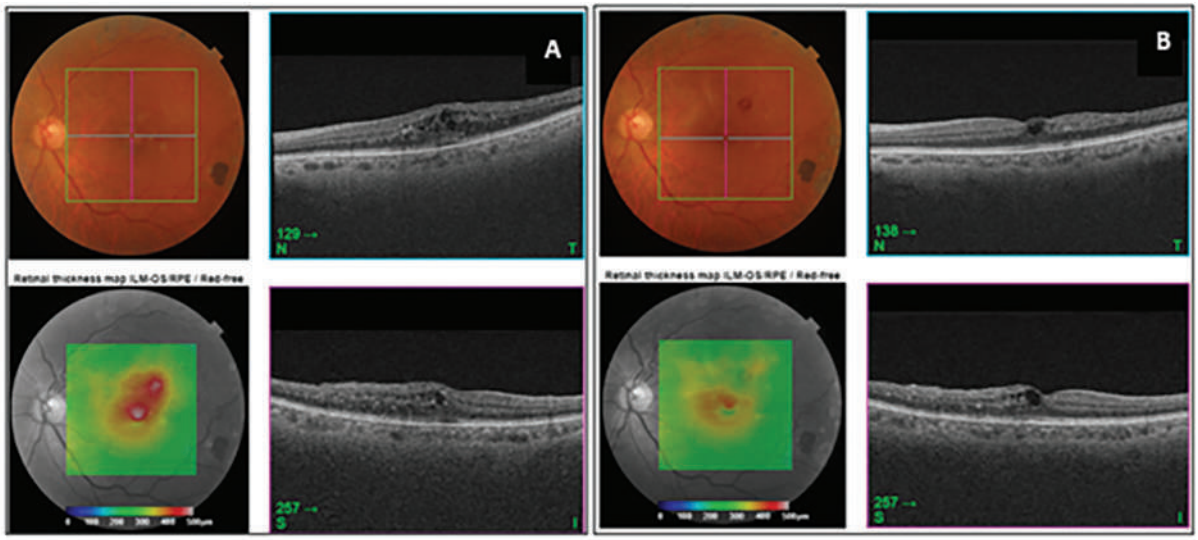


A. Right eye at presentation (March 2024): neuroepithelial detachment in the macular region, best-corrected visual acuity 0.4 Snellen, central macular thickness 194 µm. **B.** Right eye after 2 months of CHC therapy (May 2024): complete resolution of the sub-retinal fluid in the macular region, best-corrected visual acuity 0.8 Snellen, central macular thickness 174 µm.

with a sudden decline in vision in LE on February 2024. BCVA at the time of the initial visit was 1.0 in the RE and 0.1 in the LE, with no improvement possible despite refractive correction. The patient reported no prior ocular pathologies in RE, and examination showed findings within normal limits in the same eye. However, OCT (Topcon Corporation, Tokyo, Japan) imaging of the LE revealed cystoid MO secondary to a branch RVO, with a CMT of 453 µm (Figure 5A). IOP (integrated blow tonometer in the Tonoref III autorefractometer; Nidek Co., Ltd, Gamagori, Japan) was recorded at 17 mmHg in the RE and 16 mmHg in the LE. The patient was started on CHC tablets (one tablet twice daily), and systemic therapy for hypertension and dyslipidaemia was continued. No additional ocular treatments were initiated.

At the first follow-up visit on March 2024, BCVA in the RE remained stable at 1.0, whilst the LE showed no improvement, remaining at 0.1. OCT revealed a reduction in MO, with CMT reduced to 351 µm. A small neuroepithelial detachment was noted in the LE. IOP was stable at 16 mmHg bilaterally. The patient was advised to continue CHC at the same dosage.

Figure 5. Optical coherence tomography examination in cystoid macular oedema secondary to a branch retinal vein occlusion.



A. Left eye at presentation (February 2024): best-corrected visual acuity 0.1 Snellen and central macular thickness 453 µm. **B.** Left eye after 4 months of CHC therapy (June 2024): reduction of macular oedema, best-corrected visual acuity 0.5 Snellen and central macular thickness 293 µm.

By the second follow-up in June 2024, the patient showed significant improvement in BCVA in the LE, increasing to 0.5, whilst BCVA in the RE remained stable at 1.0. OCT confirmed further reduction of MO in the LE, with CMT reduced to 293 µm (Figure 5B). No recurrence of neuroepithelial detachment was noted. IOP remained within normal limits (14 mmHg in the RE and 16 mmHg in the LE). CHC therapy was continued, and no adverse effects were reported.

The patient was scheduled for a further follow-up in 2 months to monitor for potential recurrence or complications. This case highlights the potential of CHC to significantly reduce MO and improve visual function in a patient with cystoid MO secondary to branch RVO.

CHC for the management of chronic CSC

Case 1

A 53-year-old man with a history of chronic CSC (intended as CSC persistent for more than 3 months) in the LE presented in October 2022 for an ophthalmic examination. The patient had been undergoing treatment with eplerenone. BCVA was 0.2 in the RE and 0.7 in the LE. OCT (Heidelberg Spectralis) and FAG imaging confirmed a focal point of fluid leakage in the LE, whilst the peripheral retina remained normal in the RE (Figure 6A). IOP (Goldmann applanation tonometer) was recorded at 12 mmHg in both eyes. CSC was noted to be chronic. The patient was advised to start a course of CHC (two tablets daily) and was scheduled for a follow-up visit with the potential addition of micro-pulsed laser treatment in the LE if required.

At the first follow-up in December 2022, OCT imaging of the macula showed stable findings in the RE and a significant reduction in sub-retinal fluid in the LE. The patient continued the CHC regimen (two tablets daily) for another 30 days, followed by a reduction to one tablet daily for an additional 30 days until the next follow-up.

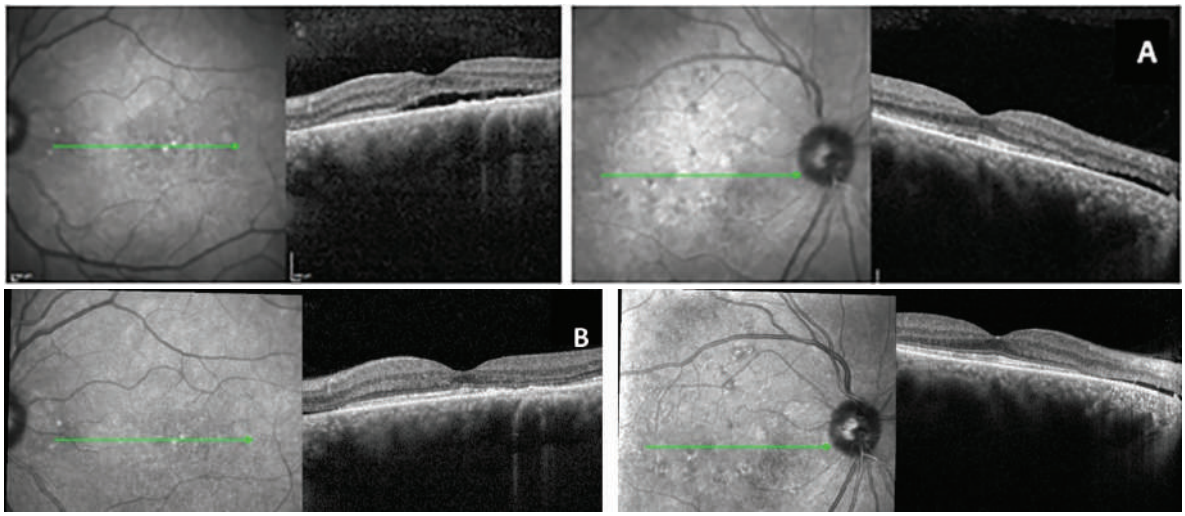
In February 2023, the second follow-up visit revealed stable OCT results for the RE and a further reduction in sub-retinal fluid in the LE. The patient was maintained on one tablet of CHC daily for 30 more days.

By March 2023, complete resolution of the MO in the LE was achieved, as confirmed by OCT (Figure 6B). The patient was instructed to return for a 3-month follow-up and continue the CHC regimen.

In June 2023, OCT demonstrated stability in the LE, with normal retinal thickness and morphology. However, the RE exhibited a small amount of residual fluid. Despite fluid in the RE, no new interventions were added. The patient was scheduled for a 6-month follow-up.

At the November 2023 visit, OCT revealed stability in the RE but the LE showed a small recurrence of sub-retinal

Figure 6. Optical coherence tomography examination in chronic central serous chorioretinopathy, case 1.



A. Focal point of fluid leakage in left eye. **B.** Complete resolution of the oedema in left eye and stability of right eye after 5 months of CHC therapy.

fluid. The patient was advised to continue CHC (two tablets daily), and a follow-up was scheduled in 2 months.

During the December 2023 follow-up, OCT showed stable results for the RE but an increase in sub-retinal fluid in the LE was noted. It was decided to evaluate the need for micro-pulsed laser therapy in the next visit. The patient was continued on CHC at the same dosage until the next evaluation.

At the most recent follow-up in January 2024, the patient's OCT findings showed stability in the RE and a slight reduction in sub-retinal fluid in the LE. The decision was made to delay the micro-pulsed laser treatment, and the patient was instructed to continue taking one tablet of CHC daily, with a follow-up planned in 2 months.

This case report highlights the role of CHC in the management of chronic CSC, with intermittent episodes of recurrence and resolution of sub-retinal fluid, ultimately postponing more invasive treatments such as micro-pulsed laser therapy.

Case 2

A 50-year-old woman with a history of profound amblyopia in the LE and myopic fundus changes presented with a sudden decrease in vision in October 2021. BCVA was 0.5 in the RE and 0.1 in the LE. Ophthalmic examination revealed deep retinal pigment epithelium (RPE) detachment in the RE, whilst the LE showed typical myopic fundus findings with a history of prior vitrectomy. OCT (Heidelberg Spectralis) confirmed RPE detachment with neuroepithelial detachment in the RE, leading to the diagnosis of chronic CSC (Figure 7A). IOP (Goldmann applanation tonometer) was 16 mmHg in both eyes. The patient was prescribed CHC (two tablets daily) and scheduled for a follow-up after 30 days.

At the first follow-up in November 2021, OCT showed a reduction in sub-retinal fluid in the RE, with stable parafoveal RPE detachment. The patient continued taking CHC (one tablet daily) until the next control.

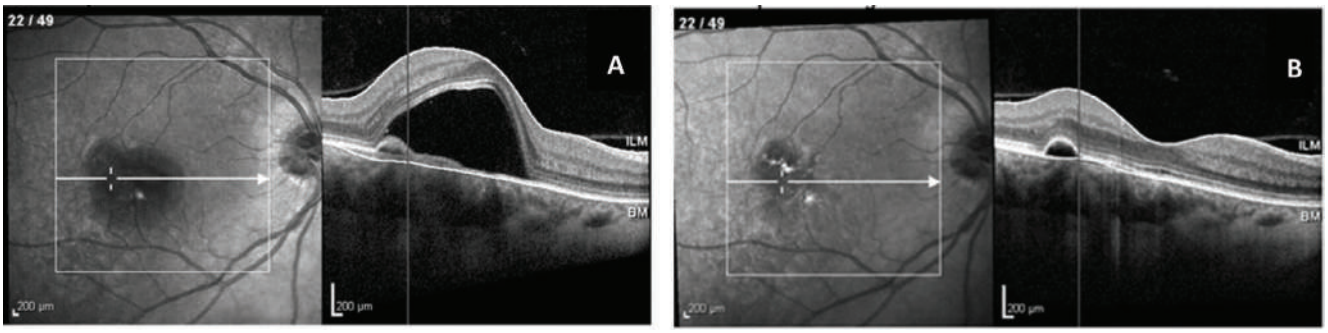
In February 2022, the patient underwent micro-pulsed laser treatment, with the follow-up scheduled 1 month later. CHC therapy (one tablet daily) was maintained during this period.

By April 2022, OCT confirmed stable clinical and tomographic findings in the RE, with no further fluid accumulation. The patient's condition remained stable, and no changes were made to her treatment.

In January 2023, OCT revealed a slight reduction in the residual fluid, confirming the stability of the condition. At the October 2023 follow-up, OCT demonstrated continued clinical and tomographic stability in the RE (Figure 7B). The patient maintained good BCVA and retinal stability for nearly 2 years with the combination of CHC and micro-pulsed laser therapy.

This case illustrates the effective long-term management of CSC with the synergistic use of CHC and laser therapy, achieving sustained vision improvement and disease stabilization.

Figure 7. Optical coherence tomography examination in chronic central serous chorioretinopathy, case 2.



A. Retinal pigment epithelium and neuroepithelial detachment in right eye at presentation, leading to the diagnosis of chronic central serous chorioretinopathy (persistent for more than 3 months). **B.** Reduction in sub-retinal fluid in right eye, with stable parafoveal retinal pigment epithelium detachment after 15 months from diagnosis and treatment with a combination of CHC and micro-pulsed laser therapy.

Case 3

A 54-year-old woman, during a follow-up eye exam in February 2024, presented decreased vision in her LE. VA was 1.0 in the RE and 0.7 in the LE. Spectral-domain OCT (Heidelberg Engineering, Inc., Heidelberg, Germany) and FAG imaging showed multiple focal points of fluid leakage in the LE with deep RPE detachment and sub-retinal fluid in OCT; this was the first presentation of CSC. The RE was normal both on ophthalmic examination, FAG and OCT. IOP (Icare HOME; TA022, Icare Oy, Vanda, Finland) was 16 mmHg in the RE and 13 mmHg in the LE. The patient was prescribed bromfenac eye drops two times a day until OCT control.

In July 2024, the patient underwent an OCT control at our centre; despite therapy with bromfenac eye drops, sub-retinal fluid was still present with detachment of the neuroepithelium, stable compared to the previous check-up in February 2024, leading to the diagnosis of chronic CSC (Figure 8A). The patient was prescribed CHC (one tablet twice daily), without continuing with other eye treatments and continued with one tablet 1 day after the first month until the OCT check, scheduled after 3 months.

At the eye check in October 2024, the patient presented a clear reduction of the sub-retinal fluid and the neuroepithelial detachment (Figure 8B) with an increase of VA at 1.0 in the LE. Eye examination and OCT showed a stable and normal appearance in the RE. She also reported good compliance and tolerability to the therapy.

This case highlights the efficacy and tolerability of CHC therapy in the treatment of chronic CSC, even in the absence of other associated therapies.

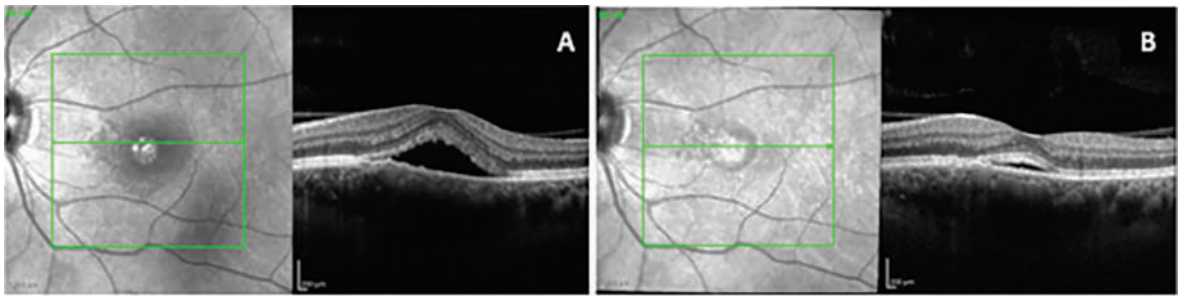
Discussion

This collection of clinical experiences supports the potential utility of a hydrophilic curcumin-based formulation (CHC, Diabec®) in managing MO across various underlying retinal pathologies. Observed findings align with emerging literature, suggesting that CHC can serve as an effective adjunct to conventional therapies, promoting both functional and anatomical improvements in patients with MO due to DR, RVO or CSC.

In particular, our findings are in line with the study by Parravano et al.,[12] who showed that adding CHC to intravitreal dexamethasone significantly enhanced the reduction of CMT in patients with DMO compared to intravitreal dexamethasone alone. This study particularly highlighted the greater efficacy of CHC in patients with early-stage diabetes and subfoveal neuroretinal detachment, conditions where inflammation plays a prominent role.[12] Similarly, Ferrara et al.[14] reported a 74% resolution rate of MO in patients with DMO treated with CHC, noting significant improvements in both BCVA and CMT. These outcomes mirror the improvements seen in our cases, particularly the marked reduction in macular thickness and the stabilization of visual function. In our series, CHC was also effective in reducing sub-retinal fluid and improving visual acuity in agreement with the literature.[14]

The ability of CHC to treat CSC can likely be attributed to its anti-inflammatory and antioxidant properties, which target the pathophysiological mechanisms of fluid leakage and RPE dysfunction. We acknowledge that chronic CSC may resolve spontaneously. However, in our cases, the resolution occurred after the initiation of CHC therapy, often following prolonged persistence or recurrence of sub-retinal fluid. This timing suggests a likely contribu-

Figure 8. Optical coherence tomography examination in chronic central serous chorioretinopathy, case 3.



A. Presence of the sub-retinal fluid and the neuroepithelial detachment in left eye. **B.** Marked reduction in sub-retinal fluid and neuroepithelial detachment in left eye after 3 months of treatment with CHC alone.

tion of CHC to the anatomical and functional improvements observed. The inhibition of the VEGF pathway and modulation of inflammatory cytokines, including TNF and IL-6, by curcumin, have been documented in several preclinical studies.[15–17]

Patient one presented with Irvine–Gass syndrome following cataract surgery and showed a complete resolution of MO after 3 months of CHC treatment. This aligns with the findings of Ferrara et al., who reported similar success in 70% of patients with post-operative MO.[14] Given that post-operative MO is primarily driven by inflammation, CHC's potent anti-inflammatory action likely played a central role in resolving the condition.

Across all cases, CHC was well tolerated, with no adverse events reported. This aligns with available evidence reporting the safety of CHC, with no significant side-effects or changes in IOP, also over long-term follow-up periods.[13,18]

This paper presents some limitations that must be acknowledged. This case series is retrospective, with a small sample size, which limits the generalizability of the findings. Moreover, without a control group, direct comparisons to standard treatments, such as anti-VEGF agents or corticosteroids, are not possible. Future prospective studies with larger sample sizes and longer follow-up periods are needed to better understand the long-term efficacy and safety of CHC in the management of MO.

Conclusion

The use of a hydrophilic curcumin-based formulation (CHC) appears to be an effective and safe option for managing MO associated with various retinal conditions. Accordingly, our collection of clinical cases highlights its potential to improve both anatomical and functional outcomes, particularly in chronic or refractory cases of MO. In conclusion, collected evidence further supports the anti-inflammatory and antioxidant properties of CHC, making CHC a viable therapeutic option or adjunctive therapy to standard treatments for the management of MO. According to the current summary of product characteristics, the recommended dosage for CHC is one tablet twice daily for acute inflammatory retinal conditions, and one to two tablets daily for chronic retinal diseases.

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