

Supplementary Materials: *In Vivo* Efficacy of Contact Lens Drug-Delivery Systems in Glaucoma Management. A Systematic Review

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Table S1. Clinical studies included in the systematic review.

Author	Year	Study Design	Sample	Ocular Assessments	Outcomes	Level	Strength	Grade
North, D.P.	1971	Letter to the editor	2 human beings	To report two case of ACG treated with CL soaked with 4% pilocarpine.	Soaked lens can be a therapeutic device in ACG.	5	IV	Very low
Podos, S.M.	1972	Prospective case series	10 human beings	To determine the pilocarpine uptake and release characteristics of soaked CL with 0.5% pilocarpine.	Pilocarpine was totally eluted from soaked CL during four hours of wear.	4	III	Low
Hillman, J.S.	1974	Case-control study	47 human beings	To assess the efficacy of 1% pilocarpine-soaked CL. in the management of acute ACG and to compare it with the traditional Intensive pilocarpine regime.	Pilocarpine-soaked CL is as effective as intensive medication with 4% pilocarpine in acute ACG	4	III	Low
Ruben, M.	1975	Retrospective case series	2 human beings	To report 4% pilocarpine-soaked CL treatment.	CL present a management problem that can be used only for selected cases.	5	III	Low
Schultz, C.L.	2009	Prospective case series	3 human beings	To evaluate clinical feasibility and toxicity of soaked CL with containing timolol maleate or brimonidine tartrate.	Patient data showed that use of the lenses maintained IOP at levels equivalent to those obtained with previous treatment.	4	III	Low

ACG: angle closure glaucoma; CL: contact lens.

Table S2. Preclinical studies included in the systematic review.

Author	Year	Sample	Purpose	Outcomes	Ethical Statement	Study Design	Experimental Procedures	Experimental Animals	Housing and Husbandry	Sample Size	Allocation & Animals to Experimental Groups	Experimental Outcomes	statistical Methods	Grade
Asseff, C.F.	1973	3 rhesus monkeys	To determine the amount of pilocarpine in the aqueous humor of primates after application of 1% pilocarpine-soaked CL.	The soaked CL produced higher and more prolonged aqueous humor pilocarpine concentrations.	0	2	2	2	0	0	0	2	0	Moderate
Hiratani, H.	2005	4 Nippon albino rabbits	To evaluate molecularly imprinted CL for delivering timolol.	The molecular imprinting technique provides CL with higher drug loading capacity.	1	2	2	2	2	0	0	2	2	Very Low
Xu, J.	2009	8 Nippon albino rabbits	To develop micelles-laden CL that could achieve the sustained release of timolol and latanoprost.	The micelles-laden CL has great potential to serve as a novel sustained drug delivery system.	1	2	2	2	2	1	2	2	1	Low
Xu, J.	2010	5 New Zealand rabbits	To develop a CL for puerarin delivery.	The CL extended the retention of puerarin in the precorneal area compared to eyedrops.	1	1	2	2	2	1	2	2	1	Very low
Peng, C.C.	2012	12 beagle dogs	To demonstrate the efficacy of glaucoma therapy through release of	Inclusion of vitamin E into the lenses did not improve the IOP reduction.	2	2	2	1	1	0	0	2	2	Low

			timolol from vitamin E CL.											
Peng, C.C.	2012	10 beagle dogs	To demonstrate that incorporation in CL can increase the timolol release duration.	Incorporation of vitamin E into the lenses can significantly increase the drug release duration from a few hours to several days.	2	2	2	1	1	0	0	2	2	Low
Jung, H.J.	2013	10 beagle dogs	To develop particle loaded silicone hydro-gel materials that can be used as extended wear CL to deliver timolol.	CL loaded silicone hydro-gel materials has a slow and extended release of timolol.	1	1	2	1	1	0	0	1	0	Low
Ciolino, J.B.	2014	4 New Zealand white rabbit	To describe a CL designed to elute latanoprost for at least one month.	Latanoprost-eluting CL can deliver a therapeutic amount of drug into the eye for at least one month.	2	2	2	1	1	0	0	2	2	Very low
Hsu, K.H.	2015	10 beagle dogs	To prove the efficacy of simultaneous release of timolol and dorzolamide from CL.	Vitamin E loading increases release durations of several drugs.	2	2	2	1	1	0	0	2	2	Low
Ciolino, J.B.	2016	4 cynomolgus monkeys	To assess latanoprost-eluting CL to lower the intraocular pressure.	CL latanoprost drug delivery is effective as delivery with daily latanoprost eyedrops	0	2	2	1	0	0	2	2	2	Moderate
Maulvi, F.A.	2016	12 New Zealand rabbits	To fabricate nanoparticle-laden ring implant in CL for delivering timolol.	Pharmacodynamic data in rabbit model showed sustained reduction in intra ocular pressure for 192 hours.	2	2	2	2	2	0	1	2	0	Low

Desai, A.R.	2018	18 New Zealand white rabbits	To evaluate the efficacy of CL with two implants (timolol and hyaluronic acid).	CL with implants has a strong potential for sustained ophthalmic drugs delivery.	2	2	2	2	2	0	2	2	0	Low
Maulvi, F.A.	2019	12 New Zealand white rabbits	To investigate the effect of gold nanoparticles on timolol loading and its release kinetics from the contact lens.	Incorporating the gold nanoparticles into the CL enhances the uptake of timolol.	2	2	2	1	1	0	1	2	2	Low
Desai, A.R.	2020	18 New Zealand white rabbits	To assess the efficacy of CL with three implants (bimatoprost-timolol-hyaluronic acid).	The implantation technology allowed delivering multiple drugs for a prolonged period of time.	2	2	2	2	2	0	2	2	2	Low

CL: contact lens. Score: 0: No mentioned 1: Unclear/Not complete 2: Adequate/Clear. N/A: not applicable.