NANO DROPPER *White Paper*

Oversized eyedrops compromise glaucoma patient adherence, causing disease progression, and eventually, irreversible blindness.

Glaucoma is a leading cause of irreversible blindness worldwide.[1]

While glaucoma is treatable, there is currently no known cure for this chronic disease and once diagnosed, glaucoma patients face a lifetime of daily use of medications and/or numerous surgical procedures. Standard first-line treatment medications that lower intraocular pressure (IOP) are administered in the form of eye drops. When used as directed, daily administration of eyedrops lowers and stabilizes IOP, preventing further damage to the optic nerve and allowing patients to maintain their eyesight. However, **50-75% of glaucoma patients struggle to adhere to their prescription treatments**.[2-4]

Oversized eyedrops jeopardize glaucoma treatment adherence by increasing the incidence and severity of adverse side effects of medication.

Prescription eyedrop bottles elute drops that exceed the capacity of the human eye by five times.[5] Therefore, every time a patient administers one eyedrop they are **losing approximately 80% of their medication** to wasted overflow and/or systemic absorption. The rate at which dispensed drug solutions are drained from the eye via the tear ducts is volume-dependent, increasing linearly with instilled volume.[6] Once drained by the tear ducts, anti-glaucoma drugs can be absorbed systemically where they act on the rest of the body, often producing unfavorable systemic side effects.[7] Additionally, oversized drops increase exposure to the preservatives found in eye medications, which have been shown to cause adverse local eye symptoms such as transient blurring of vision, stinging upon administration, watering eyes, and mild redness.[8]

Small eyedrops are as efficacious as their oversized counterparts.

With so many problems caused by oversized eyedrops, smaller eyedrops have emerged as an attractive solution. And indeed, the safety and therapeutic efficacy of small eyedrops have been demonstrated in myriad research studies:

Reference	Drug	Drop volume (µL)	n =	Outcomes	Microdrops (M) vs. standard drop (S)	
					Ocular efficacy	Side effects and/or systemic absorption
File & Patton, 1980	0.5% Pilocarpine	20 vs. 50	10	Pupillary diameter (PD)	Equivalent	Fewer ocular side effects experienced with M vs. S
Petursson et al., 1984	0%, 0.25%, 0.5% Clonidine	15 vs. 70	16	Intraocular pressure (IOP), heart rate (HR), blood pressure (BP)	Equivalent	Equivalent
Miller et al., 1986	0.5% Levobunolol	20 vs. 35 vs. 50	22	IOP, HR, BP	20, 50 µL drops significantly more effective at reducing IOP than 35 µL drops	N/A
Lynch et al., 1987	2.5% Phenylephrine (PE)	8 vs. 30	11	PD	Equivalent	N/A
			17	Plasma [PE]	N/A	Less systemic absorption of M vs. S
Brown et al., 1987	2.5%, 10% Phenylephrine	8 (10% PE) vs. 32 (2.5% PE)	10	PD, plasma [PE]	M superior to S	Equivalent
Charap et al., 1989	0.5% Levobunolol	20 vs. 35 vs. 50	12	Visual acuity, IOP, resting & exercise-induced changes HR, BP	Equivalent	Less severe systemic side effects experienced with M vs. S
			117	Visual acuity, IOP, resting HR, BP	Equivalent	Equivalent
Montoro et al., 1990	0.5% Timolol	30 vs. 50	20	IOP, HR, BP	Equivalent	Less severe systemic side effects experienced with M vs. S
Craig & Griffiths, 1991	10% Phenylephrine	10 vs. 30	20	PD	Equivalent	M caused less ocular discomfort than S
Gray, 1991	1% Tropicamide + 10% PE; 1% Tropicamide; 0.5% Tropicamide	5 vs. 26	60	PD	1% Tropicamide + 10% PE: S superior to M; 1% Tropicamide: Equivalent; 0.5% Tropicamide: S superior to M	M caused less ocular discomfort than S
Gray et al., 1992	1% Tropicamide	5 vs. 26	20	Pupil:cornea diameter, visual acuity	M equivalent (pupil:cornea diameter) or superior (visual acuity) to S	N/A
Vocci et al., 1992	0.5%, 1% Apraclonidine	16 (0.5%) vs. 30 (0.5%, 1%)	29	Resting HR, BP, visual acuity, IOP	Equivalent	Less severe systemic side effects experienced with M vs. S
Whitson, 1993	10% Phenylephrine	10 vs. 30	13	PD, plasma [PE]	Equivalent	Less systemic absorption of M vs. S
Lal et al., 1995	2% Pilocarpine	10 vs. 20 vs. 40 vs. 80	12	PD, HR	M superior to S	Decreased incidence of ocular and systemic side effects with M vs. S
Elibol et al., 1997	1% Cyclopentolate; 10% PE; 0.5% Tropicamide	6 vs. 35	61	PD, HR, BP	1% Cyclopentolate,10% PE: Equivalent; Tropicamide 0.5%: S superior to M	Equivalent

NANO DROPPER is an eyedrop bottle adapter that creates smaller drops to reduce side effects in order to improve glaucoma patient adherence and outcomes.

Nanodropper is a patented, FDA listed, award-winning, universal adaptor for eyedrop medication bottles that creates smaller and more efficacious droplets to reduce medication adverse side effects in order to improve treatment adherence. **Nanodropper is available for purchase online at www.nanodropper.com**.

[1] Parihar, J.K.L., 2016. "Glaucoma: The 'Black Hole' of Irreversible Blindness." *Medical Journal Armed Forces India.* [2] Newman-Casey, PA *et al.*, 2015. "Patterns of Glaucoma Medication Adherence over Four Years of Follow-Up." *Ophthalmology.* [3] Nordstrom, B.L. *et al.*, 2005. "Persistence and Adherence With Topical Glaucoma Therapy." *American Journal of Ophthalmology.* [4] Kahook, M.Y., 2019. "Of Course I Took my Eye drops, Doctor (Improving Adherence)." *The 42nd Annual Midwest Glaucoma Symposium.* [5] Mishima, S. *et al.*, 1966. "Determination of Tear Volume and Tear Flow." *Invest Ophthalmol.* [6] Chrai, S.S. *et al.*, 1973. "Lacrimal and Instilled Fluid Dynamics in Rabbit Eyes." *Journal of Pharmaceutical Sciences.* [7] Shell, J.W., 1982. "Pharmacokinetics of Topically Applied Ophthalmic Drugs." *Survey of Ophthalmology.* [8] Jaenen, N. *et al.*, 2007."Ocular Symptoms and Signs with Preserved and Preservative-Free Glaucoma Medications." *European Journal of Ophthalmology.*