

## Current Ophthalmopharmacotherapy Needs: Beyond the Eye

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History of ophthalmopharmacotherapy starts from ancient Egypt documented in the Ebers Papyrus (ca. 1,550 B. C.) [1,2], including “drugs with undeniable pharmacologic activity, such as copper salts, calcium carbonate, sulfur, *hyoscyamus*, and *ricinus* reeds” [2]. Topical therapy of the eye diseases was commonly used at that time, dominantly presented by eye ointments with different components and honey [1]. Eye drops were used rarely [1].

A lot has changed since then.

The basics of modern ophthalmological pharmacotherapy were laid in nineteenth century [3].

Atropine as a mydriatic eye drops was developed by pharmacist Friedlieb Ferdinand Runge in 1819 [4]. Pilocarpine have been used since the 1870s for glaucoma therapy [5], but recently it was repurposed as an innovative prescription for presbyopia [6]. Increased risk of retinal detachment associated with pilocarpine was also evidenced in patients with presbyopia [7,8].

During the 20<sup>th</sup> century drug development, specifically eye drops preparation has accelerated since Second World War, incorporating also the concept of sterility [9].

Up to present topical ocular therapy of different eye diseases by eye drops remains the mainstay of *treatment* [10].

In an effort to overcome ocular structure and bio-absorption barriers, such as pre-corneal tear film, the cornea, the conjunctiva, the lacrimal drainage system, the limited volume of conjunctival fornices [11], multiple approaches have been developed [12,13].

Despite the achievements directed to increase a bioavailability of topical drugs, posterior segment disorders still represent a challenge, to overcome which was introduced intravitreal route of therapeutic agents delivery, currently in common use in age-related macular degeneration, retinal vein occlusion, diabetic retinopathy with or without macular edema. Risk of ocular: injection-related (endophthalmitis, vitreous hemorrhage, retinal detachment, etc.), chemical-compound related (macular ischemia, etc.) and systemic (arteriothrombotic events, stroke) [14] side effects could accompany intravitreal injections. Besides, some patients are refractory to anti-VEGF drugs or develop resistance deteriorating a visual outcome.

It must be taken into consideration that frequent intravitreal injections represent also an economic burden, specifically in aging population with raising numbers of patients with diabetic retinopathy, age-related macular degeneration, glaucoma.

“We face enormous challenges in avoiding vision impairment as the global population grows and ages” [15]. The forecast for the year 2040 indicates that the number of patients with age-related macular degeneration will reach 288 million [16], with diabetic retinopathy - 224 million [17], with glaucoma - 111.8 million [18], respectively.

Management of glaucoma, as a bilateral neurodegenerative disease, causing the optic neuropathy, and ending by irreversible blindness, requires not only local hypotensive therapy, but also a neuroprotection. It is noteworthy that eyes are a window to the brain, highlighting a feasibility of early diagnosis of other neurodegenerative disease, such as Alzheimer’s disease, also in need of neuroprotection.

It is well validated that age-related macular degeneration, glaucoma, and diabetic retinopathy, as a most common microvascular complication of diabetes, starting from neurovascular unit abnormality, represent diseases with bilateral involvement, which underscores a need for oral systemic therapy targeting both eyes simultaneously, as a cost-effective approach, in contrast to monocular local topical or invasive intraocular drug delivery.

### Conclusion

In conclusion, despite the advances and achievements in ophthalmopharmacotherapy, there is still a room for improvement, specifically for such posterior segment disorders, as glaucoma, age-related macular degeneration, diabetic retinopathy. Millennial-minded approach should be directed to invention of noninvasive, user-friendly, accessible and affordable, versatile multitarget drug with multimodal mechanisms of action providing with a window of opportunity for the prevention of vision loss.

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